

Supporting information

Nanopalladium-Catalyzed Conjugate Reduction of Michael Acceptors – Application in Flow

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1. General information

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1. General Information

The substrates and the solvents were purchased from commercial sources and used as supplied. The silica based Pd⁰-AmP-MCF was synthesized as previously reported¹ and analysed with inductively coupled plasma (ICP-OES) for determination of palladium content, which was measured to 12wt%. ICP-OES was also used for determination of palladium content in the leaching tests. For H-Cube® hydrogenations, the catalyst (Pd⁰-AmP-MCF) was sent to Thalesnano² for filling of cartridges. Each H-Cube® cartridge (30 x 4 mm) was loaded with 70-80 mg of Pd⁰-AmP-MCF. For the Vapourtec reactor (Omnifit 6 mm column) 226-242 mg of Pd⁰-AmP-MCF was packed between plugs of celite at each end in a column. NMR spectra were recorded at 298 K using CDCl₃. Chemical shifts are reported in ppm relative to solvent peaks (¹H: CDCl₃ δ 7.26 and ¹³C: CDCl₃ δ 77.0) with multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, app. = apparent), coupling constants (in Hz) and integration. For ¹⁹F NMR the spectrum was referenced by using the deuterium signal of CDCl₃.³ GC-MS analyses were performed on an Agilent 7890GC/5975CMSD spectrometer equipped with a HP-5MS, 30 m x 0.25 mm, 0.25 μm column. For detection of the molecular mass either electron impact or field ionization was used. 1,3,5-Trimethoxybenzene was added to the reaction mixture before hydrogenation for reactions quantified by analysis of ¹H NMR spectra. For preparative experiments, benzyl benzoate has been used as reference for assay of the eluents after removal of the solvent/purification.

2. Typical procedures for hydrogenation in flow

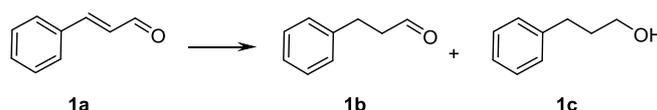
General procedure for hydrogenation using H-Cube®:

The cartridge (filled with Pd⁰-AmP-MCF) was equilibrated with EtOAc for 3 minutes under the same conditions as the hydrogenation of the substrate. A 0.1 M solution of the substrate in EtOAc was then hydrogenated at a flow rate of 1.5 mL/min, a temperature of 20 °C, and the hydrogen setting at full H₂ (30 mL H₂/min) unless otherwise stated. For completion of the hydrogenation pure solvent was flushed through the cartridge for another 3 minutes under the same conditions. For assay experiments the eluent was analyzed by ¹H NMR and for preparative experiments the solvent was removed *in vacuo* to give the products indicated in the respective experiments.

General procedure for hydrogenation using Vapourtec reactor:

The catalyst was equilibrated with EtOAc for 3 minutes under the same conditions as the hydrogenation of the substrate. A 1 M solution of the substrate in EtOAc was then passed through the column at the H₂-pressure, temperature and flow indicated for each substrate. Unless otherwise indicated a 40 psi back pressure regulator was fitted after the column. After consumption of the substrate solution the reactor was washed for 3 minutes with EtOAc under the same conditions as for hydrogenation of the substrate.

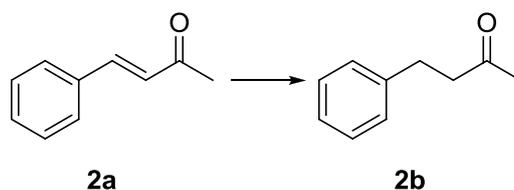
3. Detailed experimental description for substrates



3-Phenylpropanal (1b) (run in H-Cube®): A solution of cinnamaldehyde (5.33 g, 40.3 mmol) and 1,3,5-trimethoxybenzene (754 mg, 4.48 mmol) in EtOAc (403 mL) was prepared. After hydrogenation according to the general procedure the eluent was analyzed by ¹H NMR. A ratio of 85% aldehyde **1b** and 15% alcohol **1c** was found.

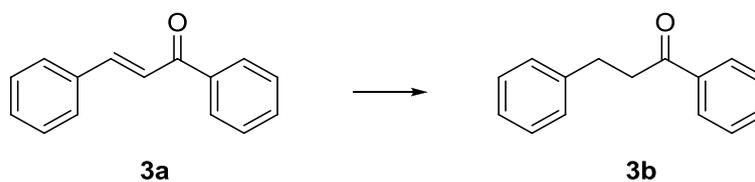
3-Phenylpropanal (1b) (run in Vapourtec): A 1 M solution was prepared by dissolving cinnamaldehyde (3.53 g, 26.7 mmol) in EtOAc (27 mL). The solution was passed through a Vapourtec reactor packed with 236 mg Pd⁰-AmP-MCF (0.266 mmol Pd) at 1 mL/min, 50 °C, and pressure of 4 bar. Full consumption of the starting material and a ratio of 6% **1c** and 94% **1b** was obtained (by ¹H NMR). Evaporation of the solvent gave 3.39 g oil which was purified over a 50 g column of silica gel using 0-40% EtOAc in heptane as eluent. After evaporation of the solvent 2.27 g (63%) **1b**. ¹H NMR (500 MHz, CDCl₃) δ 2.76 – 2.84 (m, 2H), 2.98 (app. t, *J* = 7.6 Hz, 2H), 7.19 – 7.25 (m, 3H), 7.28 – 7.34 (m, 2H), 9.84 (t, *J* = 1.4 Hz, 1H). ¹³C NMR (126 MHz, CDCl₃) δ 201.50, 140.30, 128.58, 128.26, 126.28, 45.26, 28.11. The analytical data were in agreement with those previously reported.⁴

3-Phenylpropanal (1b) (leaching test, run in Vapourtec): A solution of cinnamaldehyde (24.7 g, 187 mmol) in 162 ml EtOAc was passed through an (equilibrated) Vapourtec reactor freshly packed with 226 mg Pd⁰-AmP-MCF (0.255 mmol Pd) at 1 mL/min, 50 °C, and a H₂ pressure of 4 bar. After collection of the eluent the solvent was removed to give 25.22 g residue consisting of a mixture of **1a** (3%), **1b** (90%), and **1c** (7%). Analysis of this material showed a palladium content of 6 ppb.



4-Phenylbutan-2-one (2b) (run in H-Cube®): A 0.1 M solution of 4-phenyl-buten-2-one (0.209 g, 1.43 mmol) was made in EtOAc (14.4 mL). After hydrogenation according to the general procedure the eluent was collected and the solvent was removed *in vacuo* to give 212 mg (98%) **2b** as a colorless oil.

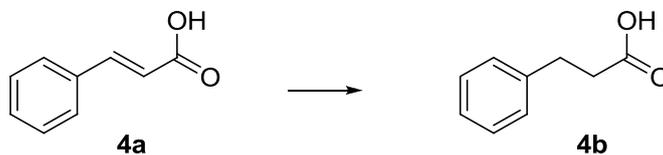
¹H NMR (500 MHz, CDCl₃) δ 2.14 (s, 3H), 2.76 (t, *J* = 7.7 Hz, 2H), 2.90 (t, *J* = 7.7 Hz, 2H), 7.16 – 7.23 (m, 3H), 7.26 – 7.31 (m, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 207.88, 140.96, 128.46, 128.26, 126.08, 45.16, 30.05, 29.72. The analytical data were in agreement with those previously reported.³



1,3-Diphenylpropan-1-one (3b) (run in H-Cube®): A solution of (*E*)-chalcone (0.299 g, 1.43 mmol) in EtOAc (14 mL) was hydrogenated according to the general procedure. After removal of the solvent the product was obtained as an oil (301 mg, 100% combined yield) containing 10 mol% 1,3-diphenylpropan-1-ol.

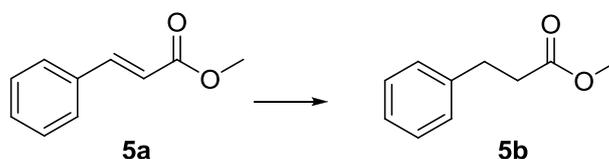
¹H NMR (500 MHz, CDCl₃) δ 3.04 - 3.11 (app. t, *J* = 7.7 Hz, 2H); 3.31 (app. t, *J* = 7.7 Hz, 2H), 7.21 (m, 1H), 7.26 - 7.34 (m, 4H), 7.46 (app. t, *J* = 7.7 Hz, 2H), 7.53 - 7.59 (m, 1H),

7.94 - 7.99 (m, 2H). ^{13}C NMR (126 MHz, CDCl_3) δ 199.36, 141.44, 137.00, 133.20, 128.75, 128.67, 128.57, 128.18, 126.28, 40.61, 30.29. The analytical data were in agreement with those previously reported.⁵



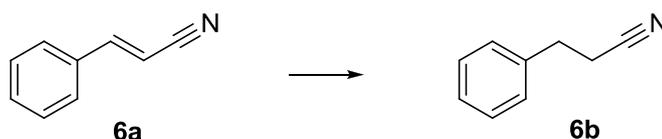
3-Phenylpropanoic acid (4b) (run in H-Cube®): A 0.1 M solution of cinnamic acid (0.206 g, 1.39 mmol) was made in EtOAc (14 mL). After hydrogenation according to the general procedure removal of the solvent gave 202 mg (97%) of the product as a colorless oil.

^1H NMR (500 MHz, CDCl_3) δ 2.69 (app. t, $J = 7.8$ Hz, 2H), 2.97 (app. t, $J = 7.8$ Hz, 2H), 7.19 - 7.24 (m, 3H), 7.28 - 7.33 (m, 2H). ^{13}C NMR (126 MHz, CDCl_3) δ 178.58, 140.11, 128.54, 128.24, 126.36, 35.48, 30.56. The analytical data were in agreement with those previously reported.³



Methyl 3-phenylpropanoate (5b) (run in H-Cube®): A 0.1 M solution of methyl cinnamate (0.235 g, 1.45 mmol) was prepared in EtOAc (14 mL). After hydrogenation according to the general procedure the eluent was collected and the solvent was evaporated to give 236 mg (99%) **5b** as an oil.

^1H NMR (500 MHz, CDCl_3) δ 2.64 (t, $J = 8.0$ Hz, 2H), 2.96 (t, $J = 8.0$ Hz, 2H), 3.67 (s, 3H), 7.16 - 7.23 (m, 3H), 7.27 - 7.33 (m, 2H). ^{13}C NMR (126 MHz, CDCl_3) δ 173.31, 140.49, 128.48, 128.24, 126.24, 51.60, 35.69, 30.93. The analytical data were in agreement with those previously reported.⁶



3-Phenylpropanenitrile (6b) (run in H-Cube®): A 0.1 M solution of cinnamonitrile (0.187 g, 1.45 mmol) was made in EtOAc (14.5 mL). After hydrogenation at a flow of 1.4 mL/min and a temperature of 30 °C the solvent was removed *in vacuo* to give 189 mg (99%) oil.

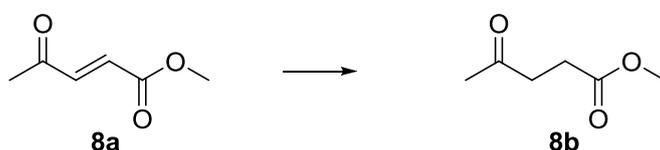
¹H NMR (500 MHz, CDCl₃) δ 2.63 (t, *J* = 7.4 Hz, 2H), 2.97 (t, *J* = 7.4 Hz, 2H), 7.22 – 7.3 (m, 3H), 7.31 – 7.37 (m, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 138.18, 129.02, 128.39, 127.38, 119.25, 31.73, 19.51. The analytical data were in agreement with those previously reported.³



Hexanal (7b) (run in H-Cube®): A 0.1 M solution of (*E*)-hex-2-enal (0.496g, 5.06 mmol) and 1,3,5-trimethoxybenzene (81.1 mg, 0.48 mmol) was made in EtOAc (51 mL). After hydrogenation at 30 °C the eluent was analyzed by ¹H NMR. A yield of 94% was indicated by assay.

Hexanal (7b) (run in Vapourtec): A column containing 226 mg Pd⁰-AmP-MCF (0.255 mmol Pd) and a 75 psi back pressure regulator fitted after the column was used. A 1 M solution of (*E*)-hex-2-enal (1.07 g, 10.9 mmol) in EtOAc (11 mL) was hydrogenated at ~6 bar in the Vapourtec reactor at a flow rate of 1 mL/min and a temperature of 50 °C. The eluent was analyzed by ¹H and ¹³C NMR, indicating complete conversion to hexanal.

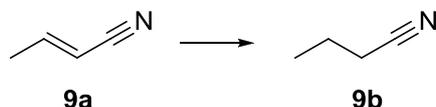
¹H NMR (500 MHz, CDCl₃) δ 0.88 (t, *J* = 7.0 Hz, 3H), 1.30 (m, 4H), 1.54 – 1.68 (m, 2H), 2.39 (td, *J* = 7.4, 1.9 Hz, 2H), 9.74 (t, *J* = 1.9 Hz, 1H). ¹³C NMR (151 MHz, CDCl₃) δ 202.55, 43.75, 31.23, 22.32, 21.66, 13.71. The analytical data were in agreement with those previously reported.⁷



Methyl 4-oxopentanoate (8b) (run in H-Cube®): A 0.1 M solution of (*E*)-methyl 4-oxopent-2-enoate (0.315 g, 2.46 mmol) in EtOAc (24 mL) was prepared. After hydrogenation according to the general procedure evaporation of the solvent gave 7b (310 mg, 97%) as an oil.

^1H NMR (500 MHz, CDCl_3) δ 2.20 (s, 3H), 2.59 (t, $J = 6.6$ Hz, 2H), 2.76 (t, $J = 6.6$ Hz, 2H), 3.68 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 206.54, 173.13, 51.72, 37.88, 29.78, 27.67.

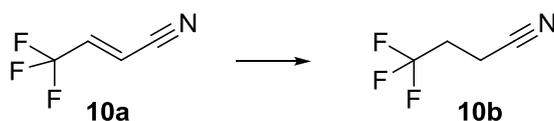
The analytical data were in agreement with those previously reported.⁸



Butyronitrile (9b) (run in H-Cube®): A 0.1 M solution of (*E*)- and (*Z*)-but-2-enitrile (0.150 g, 2.23 mmol) (ratio about 2:1) and 1,3,5-trimethoxybenzene (52.5 mg, 0.31 mmol) in EtOAc (22 mL) was prepared. After hydrogenation according to the general procedure the eluent was analyzed by ^1H NMR, indicating full conversion of starting material to **9b**.

^1H NMR (500 MHz, CDCl_3) δ 1.05 (t, $J = 7.4$ Hz, 3H), 1.67 (q, $J = 7.2$ Hz, 2H), 2.29 (t, $J = 7.1$ Hz, 2H). ^{13}C NMR (126 MHz, CDCl_3) δ 119.12, 18.80, 18.52, 12.80.

The identity of this material was confirmed by comparison with authentic material (^{13}C NMR and ^1H NMR).



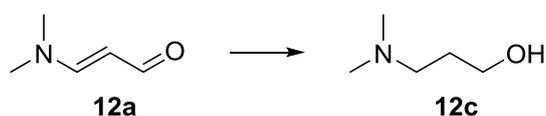
4,4,4-Trifluorobutanenitrile (10b) (run in H-Cube®): A solution of (*E*)-4,4,4-trifluorobut-2-enitrile (0.242 g, 2.00 mmol) and 1,3,5-trimethoxybenzene (68.7 mg, 0.408 mmol) was prepared in EtOAc (20 mL) and hydrogenated according to the general procedure and analyzed, 100% conversion to **10b** was indicated by assay.

Preparative (run in H-Cube®): A 0.1 M solution of (*E*)-4,4,4-trifluorobut-2-enitrile (0.3054 g, 2.52 mmol) was made in EtOAc (25 mL). After hydrogenation according to the general procedure the eluent was collected and the solvent was evaporated to give 201 mg colorless oil with an assay of 77%.

^1H NMR (500 MHz, CDCl_3) δ 2.46-2.56 (m, 2H), 2.64 (t, $J = 7.7$ Hz, 2H). ^{19}F NMR (471 MHz, CDCl_3) δ -67.40 (s, 3F). ^{13}C NMR (126 MHz, CDCl_3) δ 125.26, 116.88, (q, $J = 276.7$ Hz), 30.38, 11.20 (q, $J = 31.2$ Hz). The identity of this material was confirmed by comparison with commercial material (^1H NMR, ^{19}F NMR, and ^{13}C NMR).



3-(Dimethylamino)propanenitrile (11b) (run in H-Cube®): A 0.1 M solution of N,N-dimethylaminoacetonitrile (0.190 g, 1.97 mmol) and 1,3,5-trimethoxybenzene (88.4 mg, 0.53 mmol) was made in EtOAc (20 mL). ¹H NMR analysis of the eluent after hydrogenation according to the general procedure showed that 4% of the material had been consumed. A very weak signal corresponding to the expected mass could be observed in the GC-MS trace but ¹H NMR indicated starting material only.

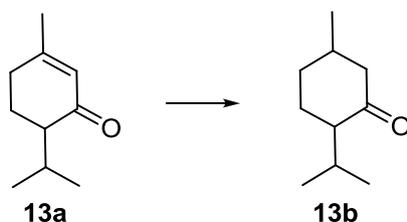


3-(Dimethylamino)propan-1-ol (12c) (run in H-Cube®): A solution of (*E*)-3-(dimethylamino)acrylaldehyde (0.566 g, 5.70 mmol) and 1,3,5-trimethoxybenzene (82.5 mg, 0.49 mmol) was made in EtOAc (57 mL). Hydrogenation at 60 °C indicated 70% 3-(dimethylamino)propan-1-ol (by assay) and 30% starting material.

Preparative (run in H-Cube®): A 0.1 M solution of (*E*)-3-(dimethylamino)acrylaldehyde (0.244 g, assay 91%) was prepared in EtOAc (22 mL). Hydrogenation at 60 °C. The solvent was removed *in vacuo* to give 153 mg colorless oil. The assay showed a purity of 77%, indicating an effective yield of 51%.

¹H NMR (600 MHz, CDCl₃) δ 1.57 – 1.74 (m, 2H), 2.23 (s, 6H), 2.51 (t, *J* = 5.9 Hz, 2H), 3.76 (t, *J* = 5.5 Hz, 2H). ¹³C NMR (151 MHz, CDCl₃) δ 64.70, 60.15, 45.55, 28.04.

The identity of this material was confirmed by comparison with commercial material (¹³C-NMR and ¹H-NMR).

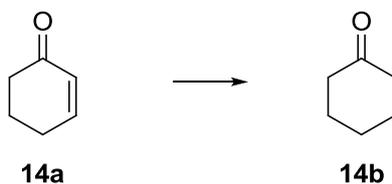


2-Isopropyl-5-methylcyclohexanone (menthone/isomenthone, 13b) (run in H-Cube®): A 0.1 M solution of 1.59 g (10.5 mmol) 6-isopropyl-3-methylcyclohex-2-enone in EtOAc (106 mL) was prepared and hydrogenated at 50 °C. The solvent was removed *in vacuo* to give 1.53 g (95%) the product as a colorless oil. ¹H NMR analysis showed two isomeric ketones (95%, the mixture consisting mainly of isomenthone) and 2-isopropyl-5-methylphenol (5%). The analytical data were in agreement with those previously reported.⁹

2-Isopropyl-5-methylcyclohexanone (menthone/isomenthone, 13b) (run in Vapourtec): A solution of 6-isopropyl-3-methylcyclohex-2-enone (4.76 g, 31.3 mmol) in EtOAc (31 mL) was prepared and passed at 30 °C through a column of Pd⁰-AmP-MCF (242 mg, 0.273 mmol) with a hydrogen pressure of 4.3 bar and a flow rate of 1 mL/min. Removal of the solvent gave 4.56 g colorless oil which consisted of a 80:15 (by GC) mixture of cis- and trans-isomeric ketones (isomenthone/menthone), 2-isopropyl-5-methylphenol (3%), and starting material (2%).

The same setup but run at a temperature of 50 °C gave a mixture of the cis- and trans-isomeric ketones (78%) and 2-isopropyl-5-methylphenol (22%).

¹H NMR (500 MHz, CDCl₃) δ 0.85 (m), 0.94 (m), 1.00 (m), 1.48 (m), 1.64 – 1.79 (m), 1.9 – 2.22 (m), 2.29 (m). ¹³C NMR (126 MHz, CDCl₃) δ 214.58, 212.40, 57.19, 55.89, 50.87, 48.03, 35.46, 34.39, 33.93, 29.43, 27.86, 26.91, 26.85, 25.89, 22.28, 21.45, 21.21, 20.89, 19.88, 18.69.



Cyclohexanone (14b) (run in H-Cube®): A solution of cyclohex-2-enone (0.238 g, 2.47 mmol) and 1,3,5-trimethoxybenzene (43.6 mg, 0.26 mmol) was made in EtOAc (25 mL). Hydrogenation according to the general procedure indicated 100 % yield by assay.

Cyclohexanone (14b) (run in Vapourtec): A solution of cyclohex-2-enone (0.97 g, 10 mmol) in EtOAc (10 mL) was prepared and passed at 20 °C through a column of 236 mg Pd⁰-AmP-MCF (0.266 mmol Pd) with a hydrogen pressure of ~3 bar and a flow of 0.5 mL/min. ¹H NMR Analysis of the eluent showed 99% cyclohexanone and 0.5% phenol.

The same setup using a flow of 1 mL/min resulted in 98% cyclohexanone and 2% phenol in the eluent. The same setup using a flow of 1 mL/min and a temperature of 50 °C resulted in 60% cyclohexanone and 40% phenol in the eluent.

Cyclohexanone (14b) (leaching test, run in H-Cube®): A solution of cyclohex-2-enone (237 mg, 2.47 mmol) in EtOAc (26 mL) was subjected to the hydrogenation conditions indicated in the general procedure. Analysis of the eluent showed a palladium content of < 2 ppb.

¹H NMR (500 MHz, CDCl₃) δ 1.70 (m, 2H), 1.83 (m, 4H), 2.30 (t, *J* = 6.7 Hz, 4H). ¹³C NMR (126 MHz, CDCl₃) δ 211.06, 41.56, 26.69, 24.68. The analytical data were in agreement with those previously reported.³

Stability test

3-Phenylpropanal (1b) (Stability test of Pd⁰-AmP-MCF in cartridge, run in H-Cube® with limited H₂): On day 1 a 0.1 M stock solution of cinnamaldehyde (3.96 g, 30 mmol) and 1,3,5-trimethoxybenzene (5.05 g, 30 mmol) was made in EtOAc (300 ml), on day 2 a 0.1 M stock solution of cinnamaldehyde (13.3 g, 101 mmol) and 1,3,5-trimethoxybenzene (1.70 g, 10.1 mmol) was made in EtOAc (1000 ml). At the start of the hydrogenations the system was primed with the resulting substrate solution at a flow of 1 mL/min, the pressure regulator set at 10 bar (controlled H₂ mode), and the temperature set at 20 °C. The eluent was sampled directly from the H-Cube® for ¹H NMR analysis after the run time indicated. The yield of product is given in relation to the internal standard. No other products could be observed in the eluents by ¹H NMR.

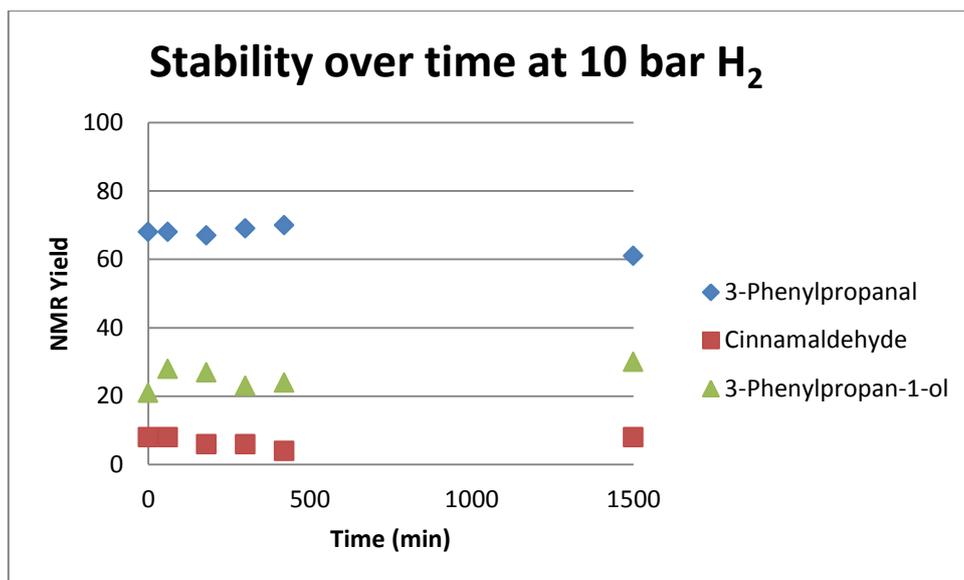


Figure 1. Stability test for Pd⁰-AmP-MCF over time, when the hydrogenation was run at 10 bar pressure of H₂.

3-Phenylpropanal (1b) (Stability test of Pd⁰-AmP-MCF in cartridge, run in H-Cube® at 50 bar): A 0.1 M stock solution of cinnamaldehyde (13.2 g, 99.6 mmol) and 1,3,5-trimethoxybenzene (1.22 g, 7.26 mmol) was made in EtOAc (1 liter). The system was primed with the resulting substrate solution at a flow of 3 mL/min for 5 minutes with no hydrogen pressure. Subsequently, the pressure regulator was set at 50 bar, the H₂ setting in controlled mode, the temperature was set at 20 °C, and the flow was set at 1 mL/min. At all times full consumption of starting material was observed. The eluent was sampled directly from the H-Cube® for ¹H NMR analysis after the run time indicated. The yield of product is given in relation to the internal standard. No other products could be observed in the eluents by ¹H NMR.

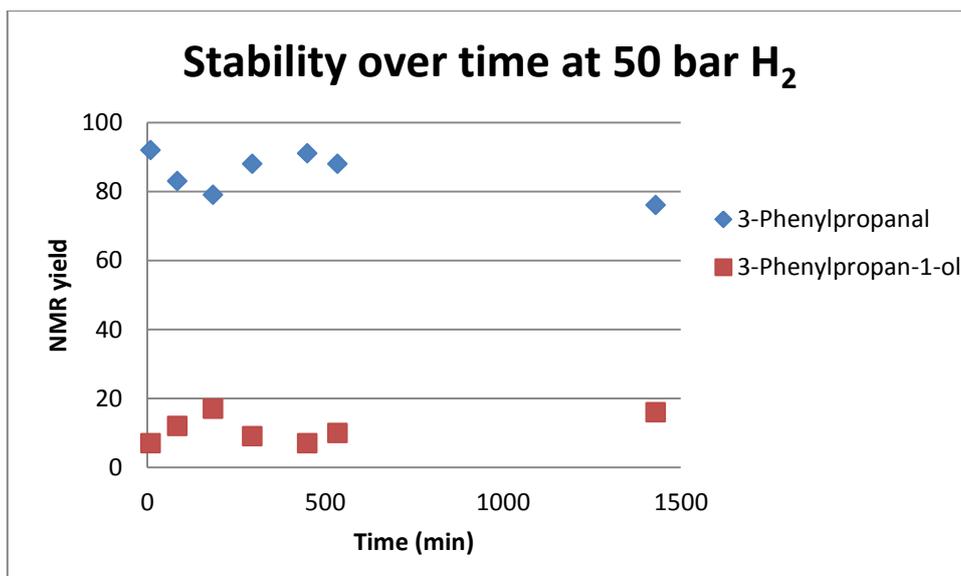


Figure 2. Stability test for Pd⁰-AmP-MCF over time, when the hydrogenation was run at 50 bar pressure of H₂.

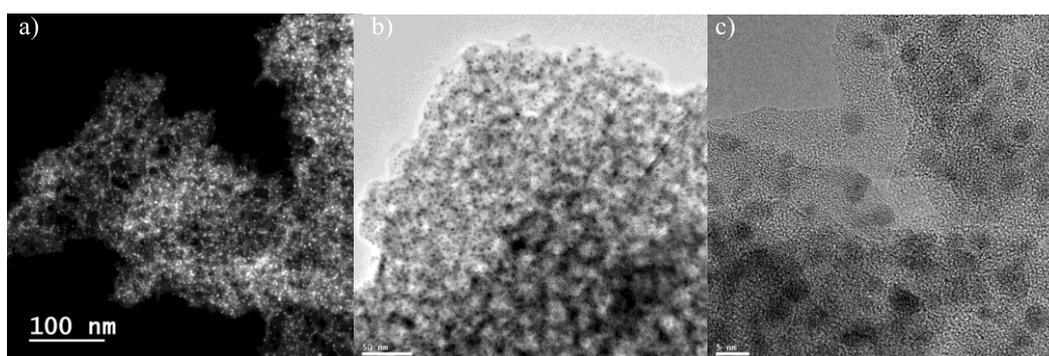


Figure 3. HAADF-STEM (a) and TEM Images (b and c) of unused Pd⁰-AmP-MCF on different scale.

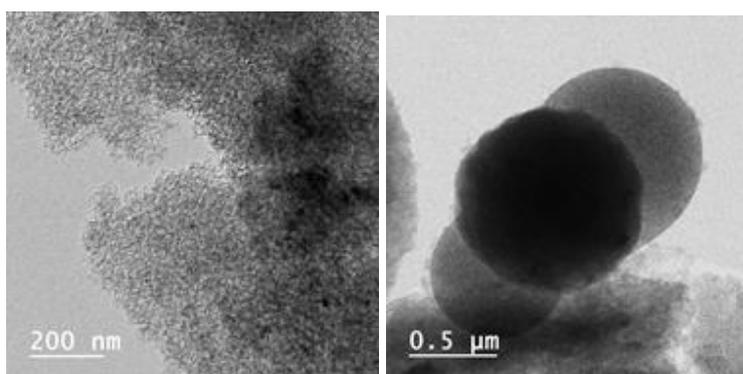


Figure 4. HAADF-STEM (a) and TEM Images (b and c) of used Pd⁰-AmP-MCF on different scale.

Schematic view of the flow devices

H-Cube®

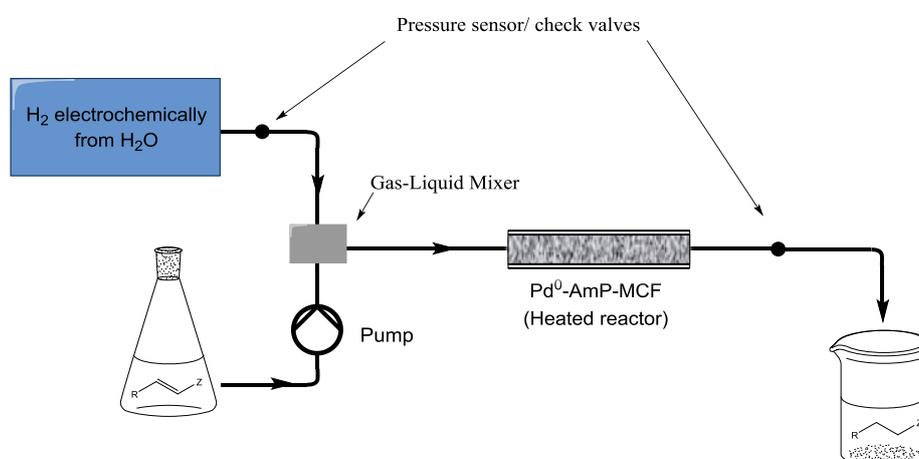


Figure 5. H-Cube® with Pre-packed cartridge with 70 mg Pd⁰-AmP-MCF (12 wt% Pd).

Vapourec

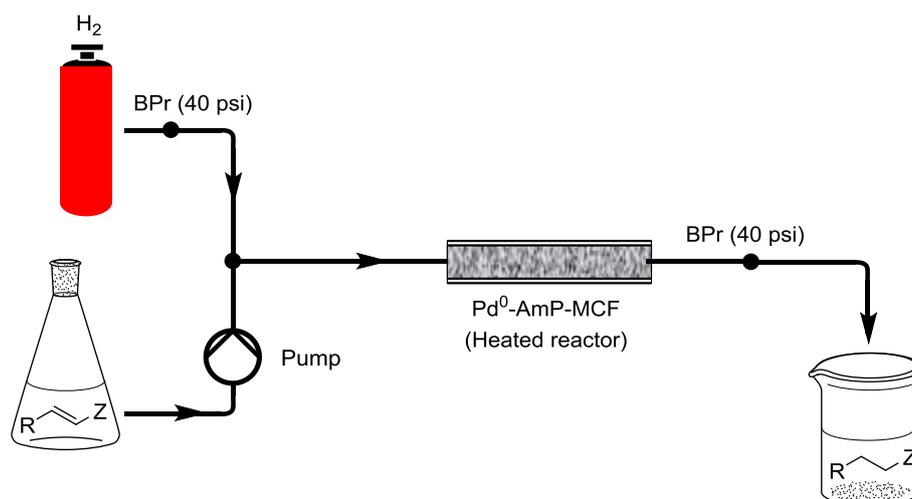


Figure 6. Schematic view of Vapourtec with 226 mg Pd⁰-AmP-MCF (12 wt% Pd).

¹ For MCF synthesis see: a) Han, Y.; Lee, S. S.; Ying, J. Y. *Chem. Mater.* **2006**, *18*, 643-649;
b) Shakeri, M.; Kawakami, K. *Micro. Meso. Mater.* **2008**, *118*, 115-120.

For loading of Pd nanoparticles and applications see: c) Johnston, E. V.; Verho, O.; Kärkäs, M. D.; Shakeri, M.; Tai, C.-W.; Palmgren, P.; Eriksson, K.; Oscarsson, S.; Bäckvall, J.-E. *Chem. - Eur. J.* **2012**, *18* (39), 12202-12206.

² ThalesNano Nanotechnology Inc., H-1031 Budapest, Zahony utca 7, Hungary

³ Gottlieb, H. E.; Kotlyar, V; Nudelman, A. *J. Org. Chem.* **1997**, *62*, 7512-7515.

⁴ Vellakkaran, M.; Andappan, M.M.S.; Kommu, N. *Eur. J. Org. Chem.* **2012**, *25*, 4694-4698.

⁵ Xu, Q.; Chen, J.; Liu, Q. *Adv. Synth. Catal.* **2013**, *355* (4), 697-704.

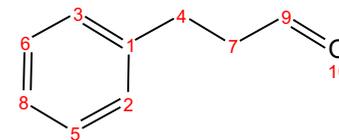
⁶ Kantam, M. L.; Kishore, R.; Yadav, J.; Sudhakar, M.; Venugopal, A. *Adv. Synth. Catal.* **2012**, *354* (4), 663-669.

⁴ Sedelmeier, J.; Ley, S. V.; Baxendale, I. R.; Baumann, M. *Org. Lett.* **2010**, *12*(16), 3618-3621

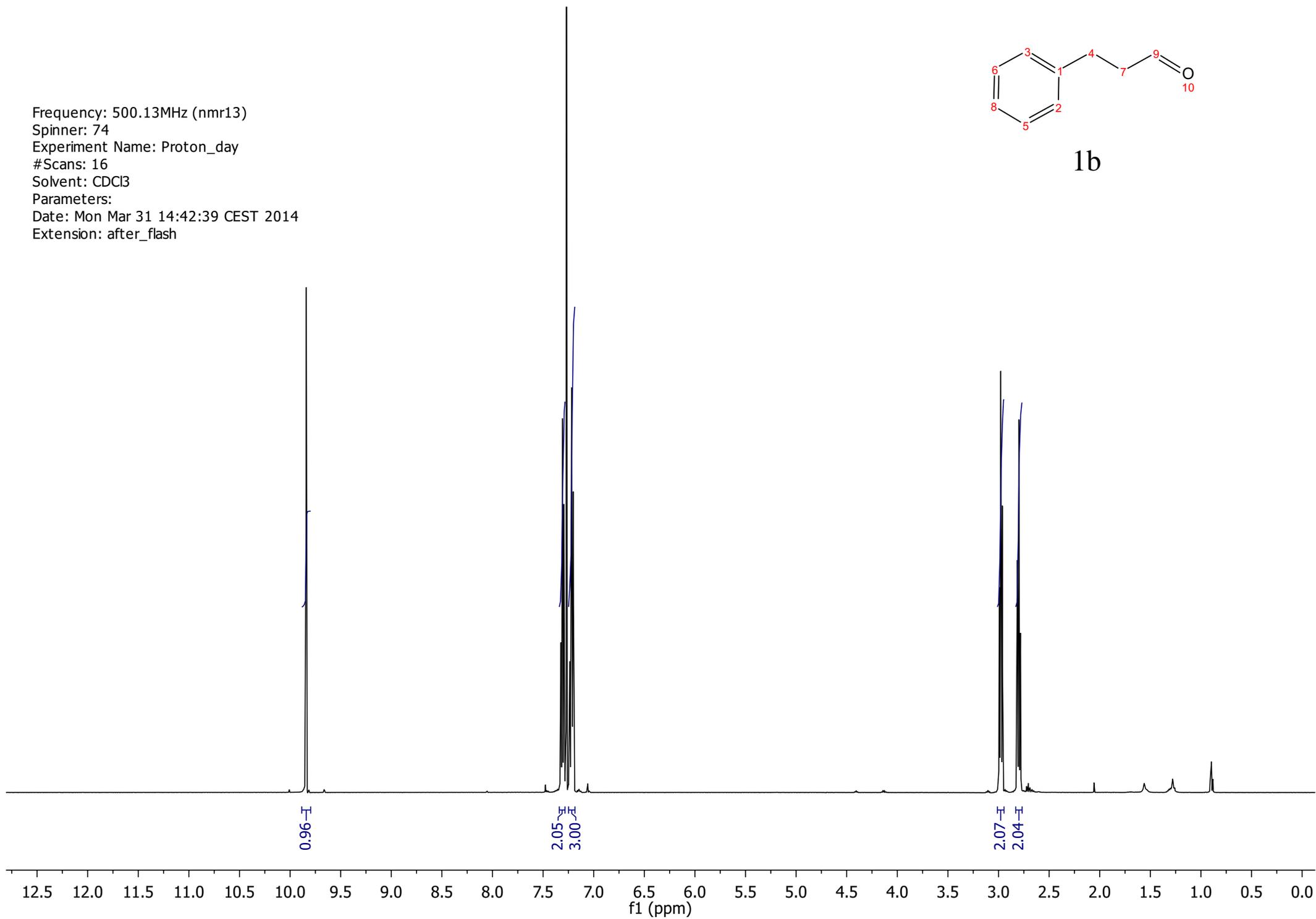
⁸ Izquierdo, J.; Rodríguez, S., González, F. V. *Org. Lett.*, **2011**, *13*(15), 3856-3859

⁹ Mosandl, A.; Köpke, T.; Benish, W. *Tetrahedron: Asymmetry* **1993**, *4* (4), 651-654.

Frequency: 500.13MHz (nmr13)
Spinner: 74
Experiment Name: Proton_day
#Scans: 16
Solvent: CDCl3
Parameters:
Date: Mon Mar 31 14:42:39 CEST 2014
Extension: after_flash



1b



—201.50

—140.30

—128.58

—128.26

—126.28

—77.25

—77.20

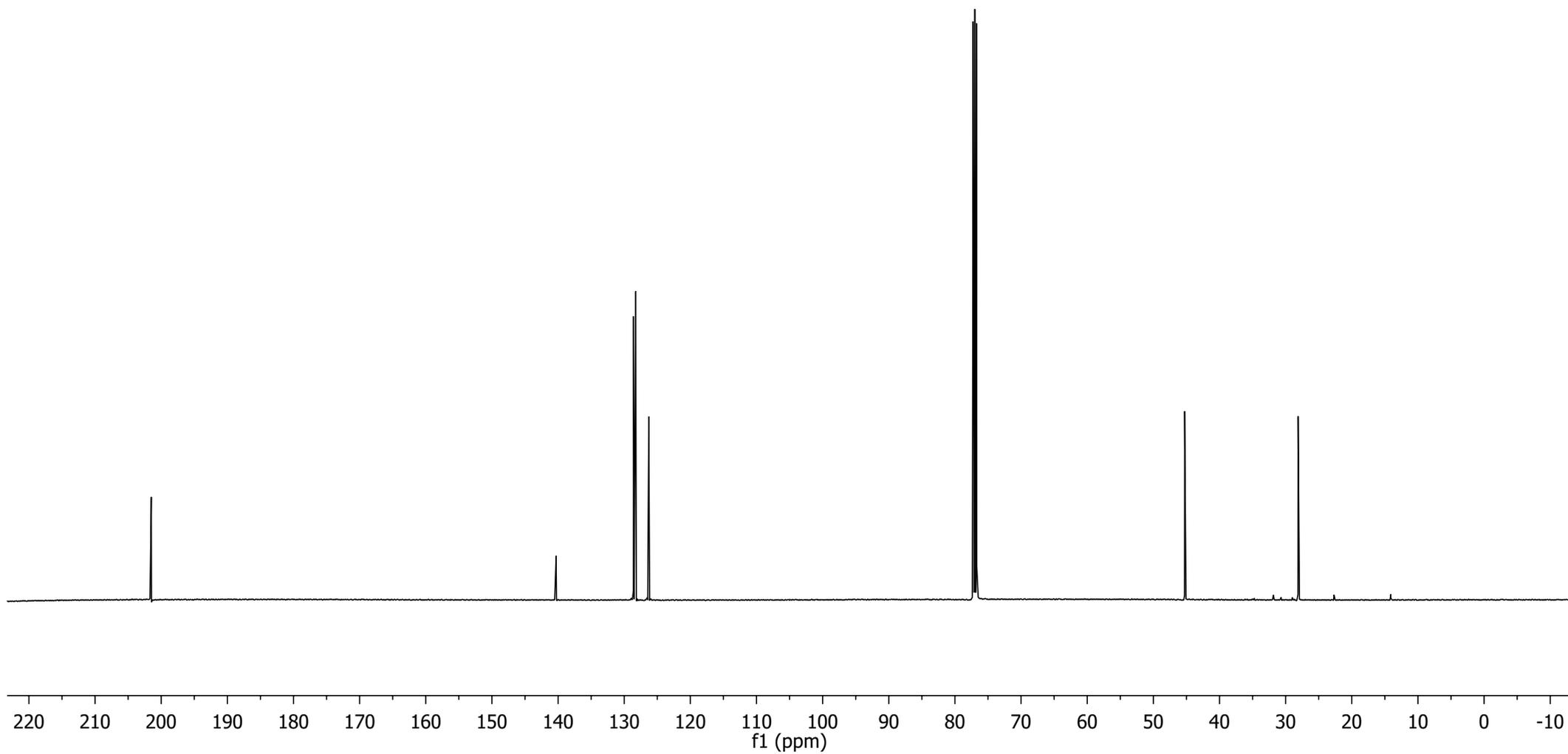
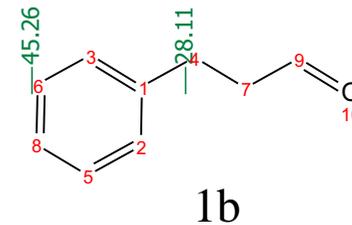
—76.99

—76.74

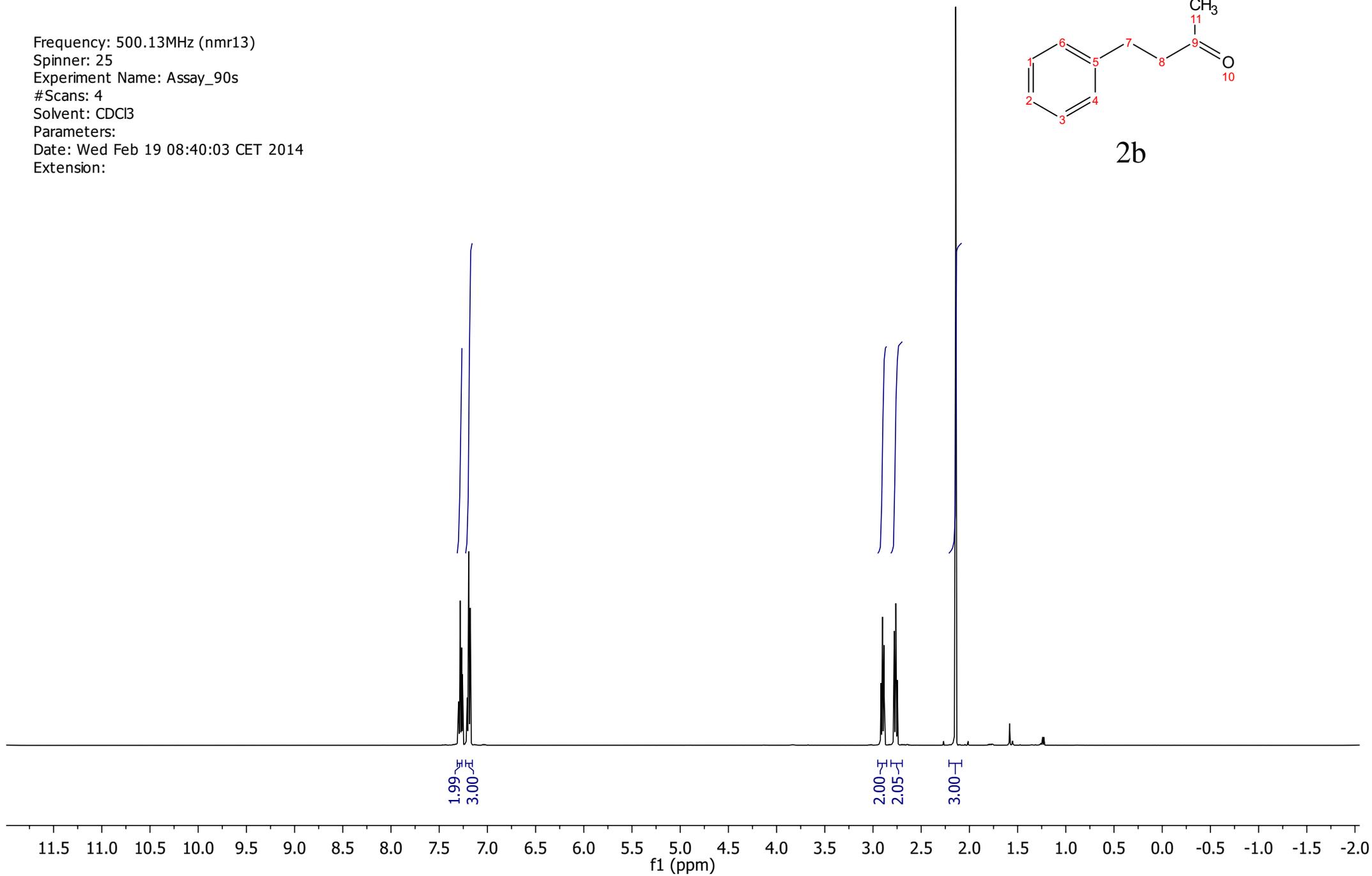
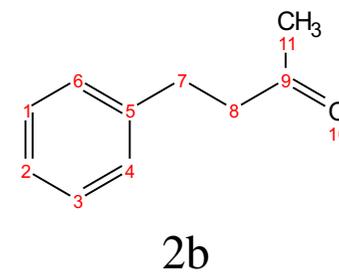
—45.26

—28.11

Frequency: 125.76MHz (nmr13)
Spinner: 74
Experiment Name: Carbon_night
#Scans: 4000
Solvent: CDCl3
Parameters:
Date: Mon Mar 31 14:42:50 CEST 2014
Extension: after_flash



Frequency: 500.13MHz (nmr13)
Spinner: 25
Experiment Name: Assay_90s
#Scans: 4
Solvent: CDCl3
Parameters:
Date: Wed Feb 19 08:40:03 CET 2014
Extension:



—207.88

—140.96

—128.46

—128.26

—126.08

—77.25

—76.99

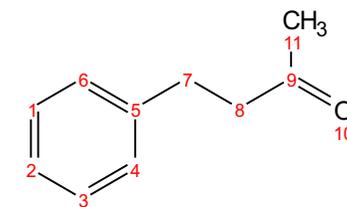
—76.74

—45.16

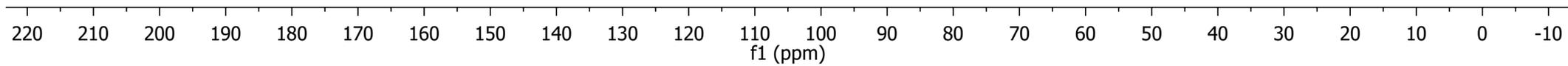
—30.05

—29.72

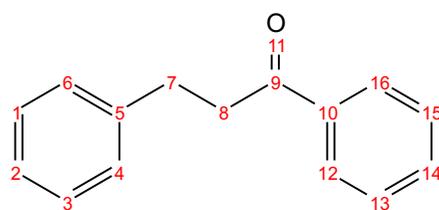
Frequency: 125.76MHz (nmr13)
Spinner: 25
Experiment Name: Carbon_night
#Scans: 4000
Solvent: CDCl3
Parameters:
Date: Wed Feb 19 11:40:12 CET 2014
Extension:



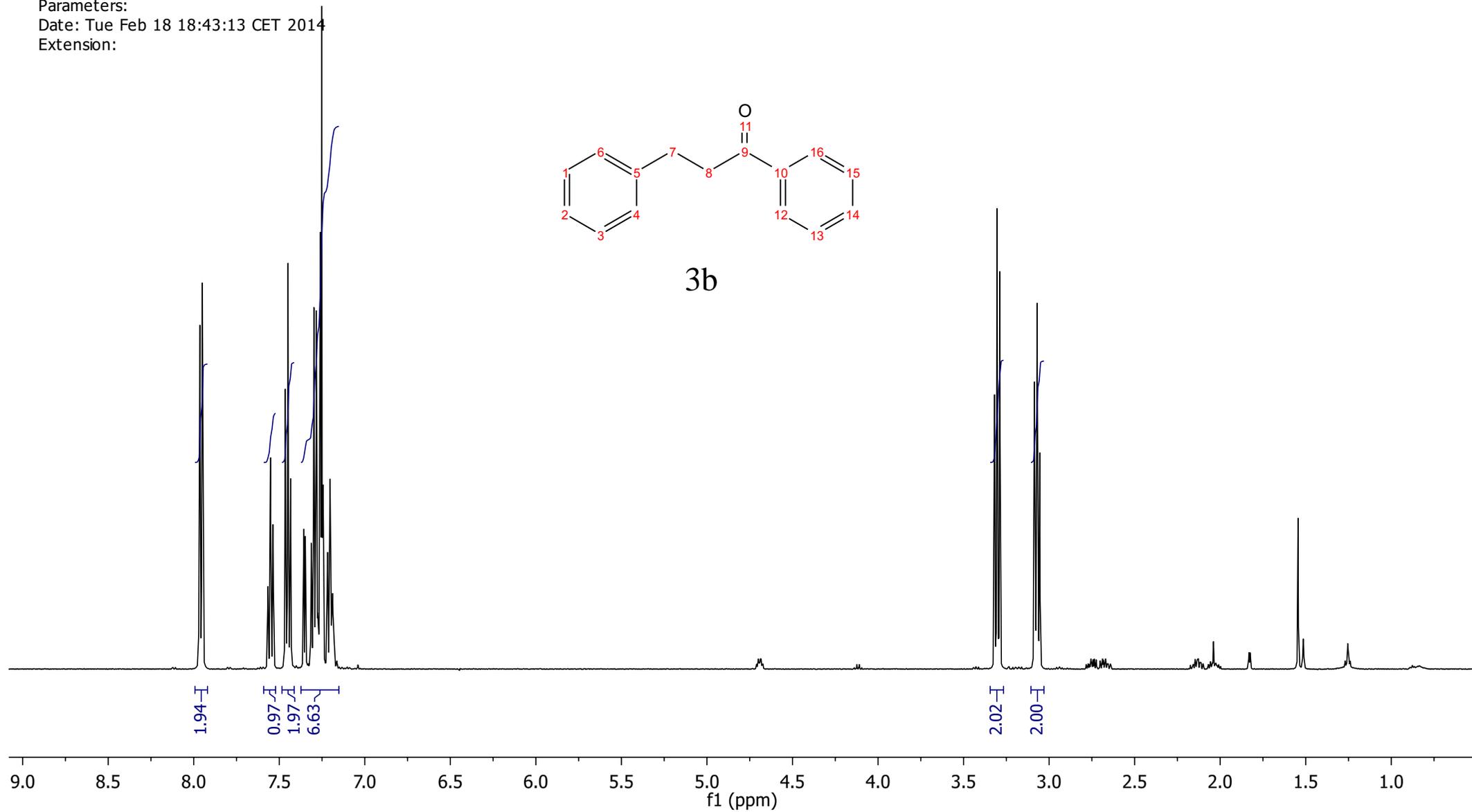
2b



Frequency: 499.96MHz (nmr9)
Spinner: 111
Experiment Name: Proton_day
#Scans: 16
Solvent: CDCl3
Parameters:
Date: Tue Feb 18 18:43:13 CET 2014
Extension:



3b



Frequency: 125.72MHz (nmr9)
Spinner: 111
Experiment Name: Carbon_night
#Scans: 4000
Solvent: CDCl3
Parameters:
Date: Tue Feb 18 18:43:29 CET 2014
Extension:

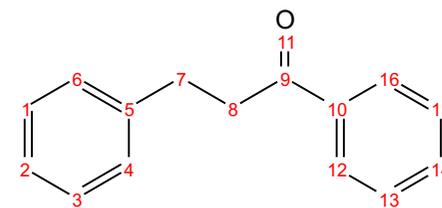
—199.36

141.44
137.00
133.20
128.75
128.67
128.57
128.18
126.28

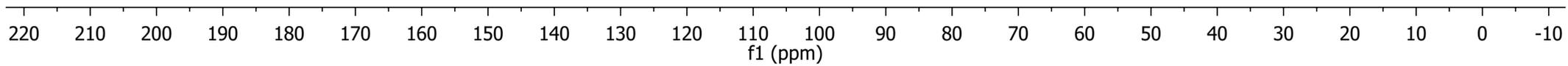
77.41
77.16
76.91

—40.61

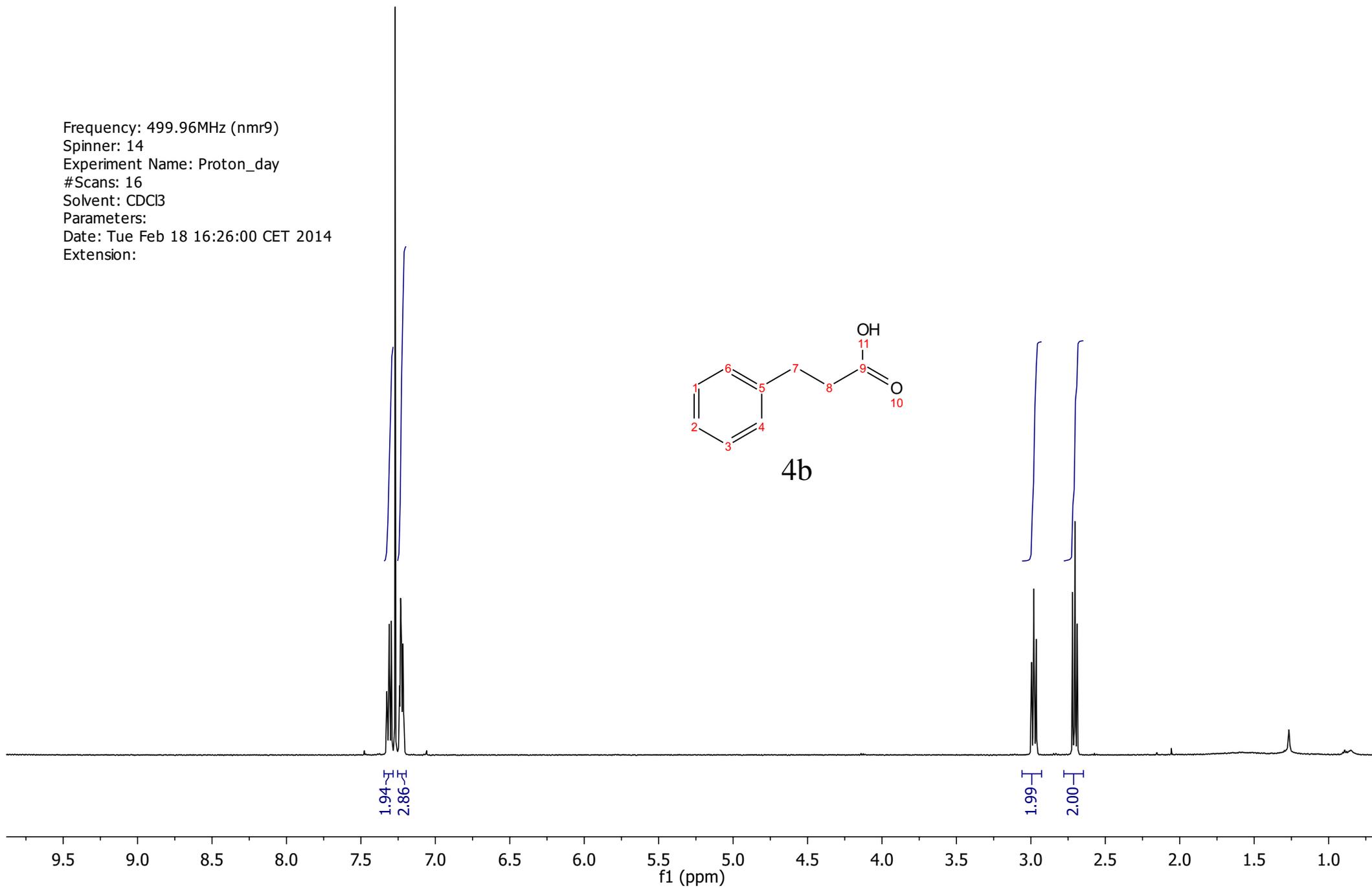
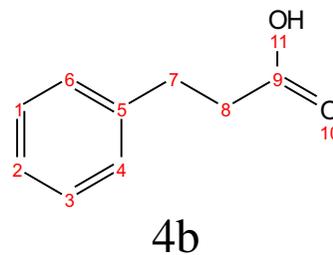
—30.29



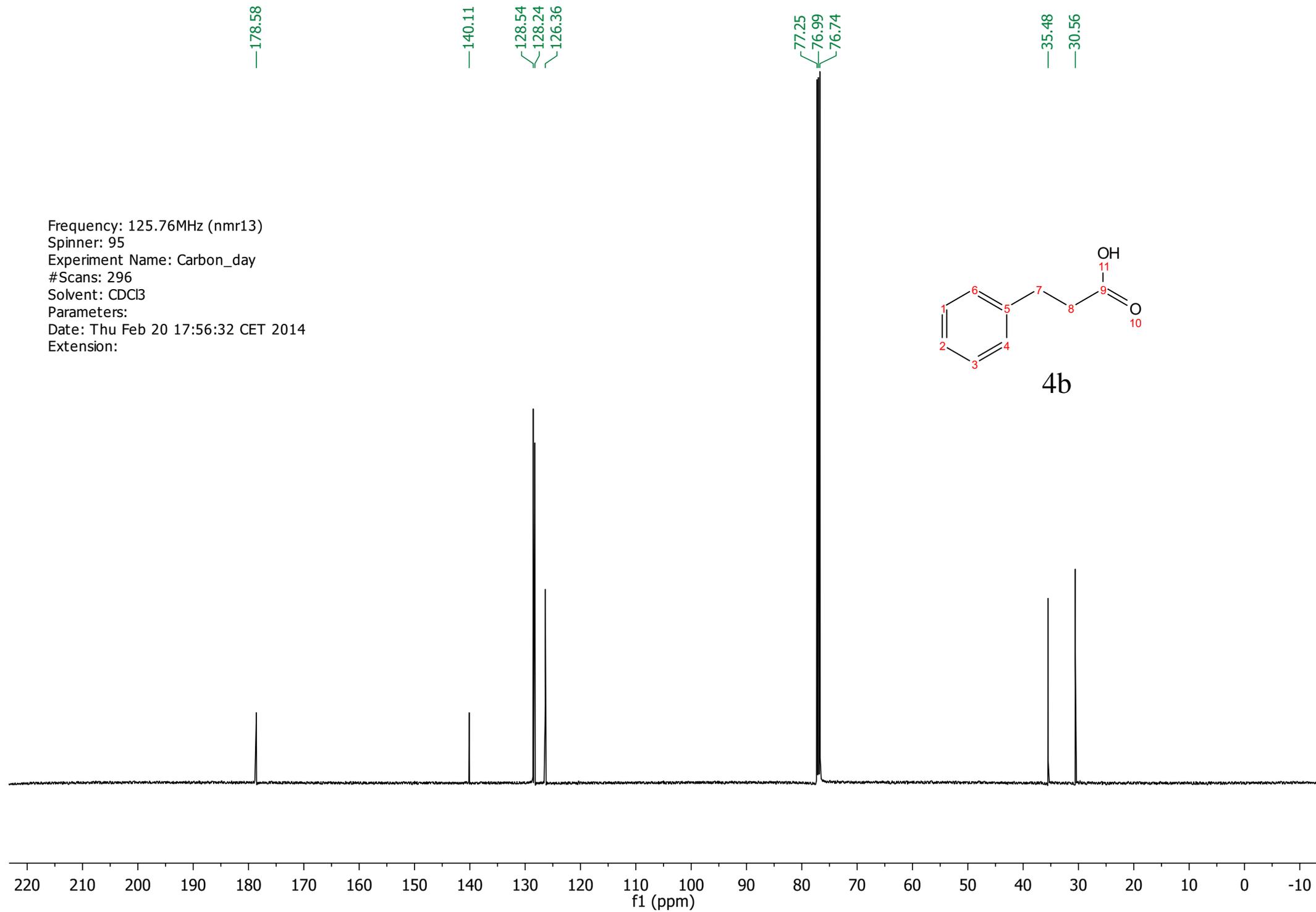
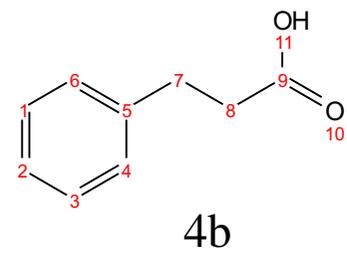
3b



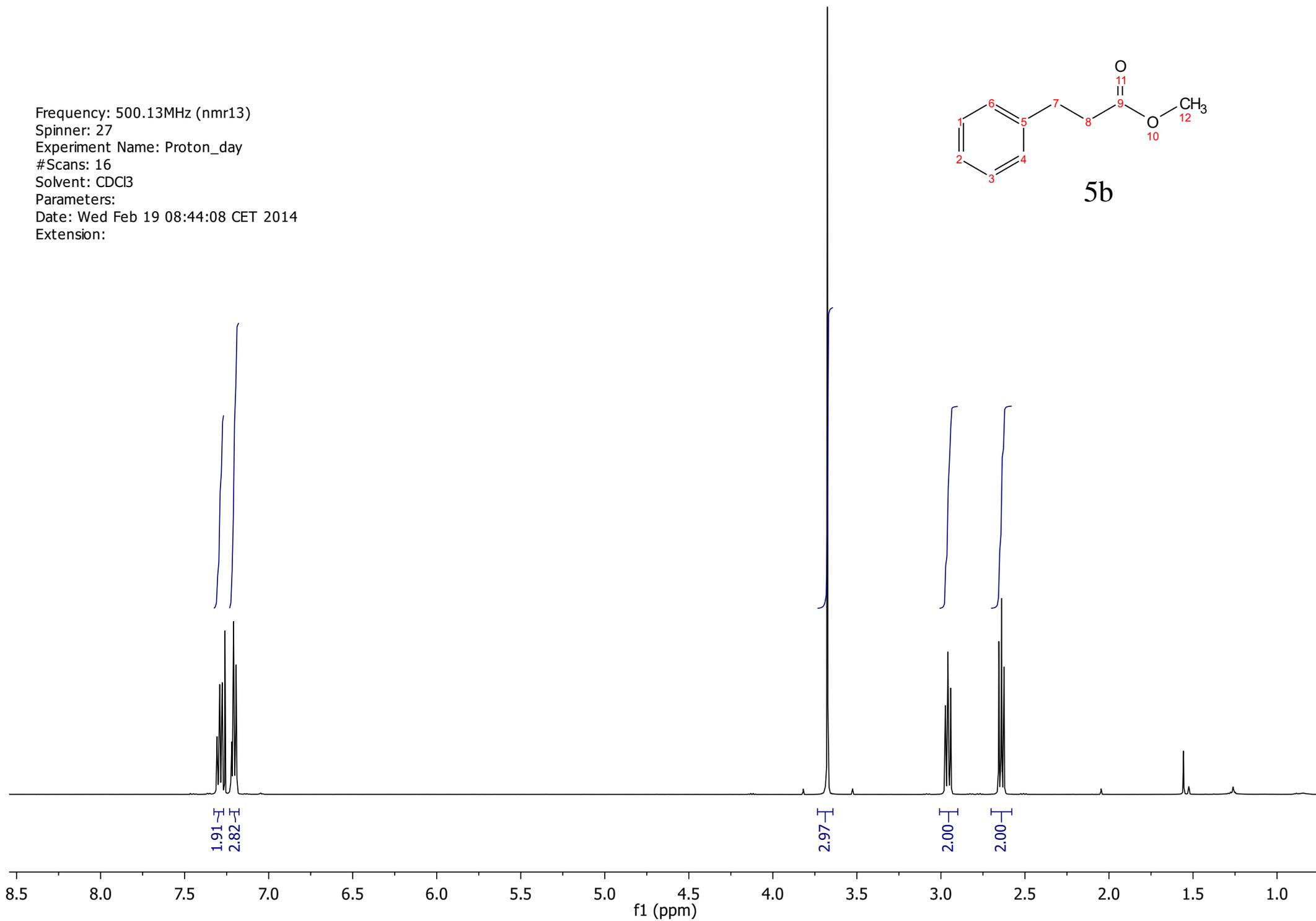
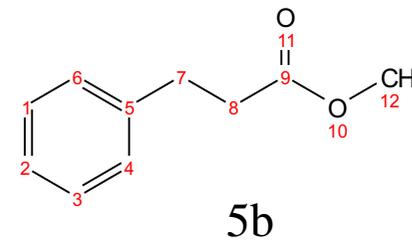
Frequency: 499.96MHz (nmr9)
Spinner: 14
Experiment Name: Proton_day
#Scans: 16
Solvent: CDCl3
Parameters:
Date: Tue Feb 18 16:26:00 CET 2014
Extension:



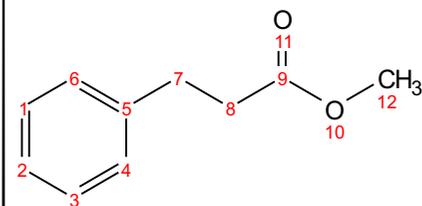
Frequency: 125.76MHz (nmr13)
Spinner: 95
Experiment Name: Carbon_day
#Scans: 296
Solvent: CDCl3
Parameters:
Date: Thu Feb 20 17:56:32 CET 2014
Extension:



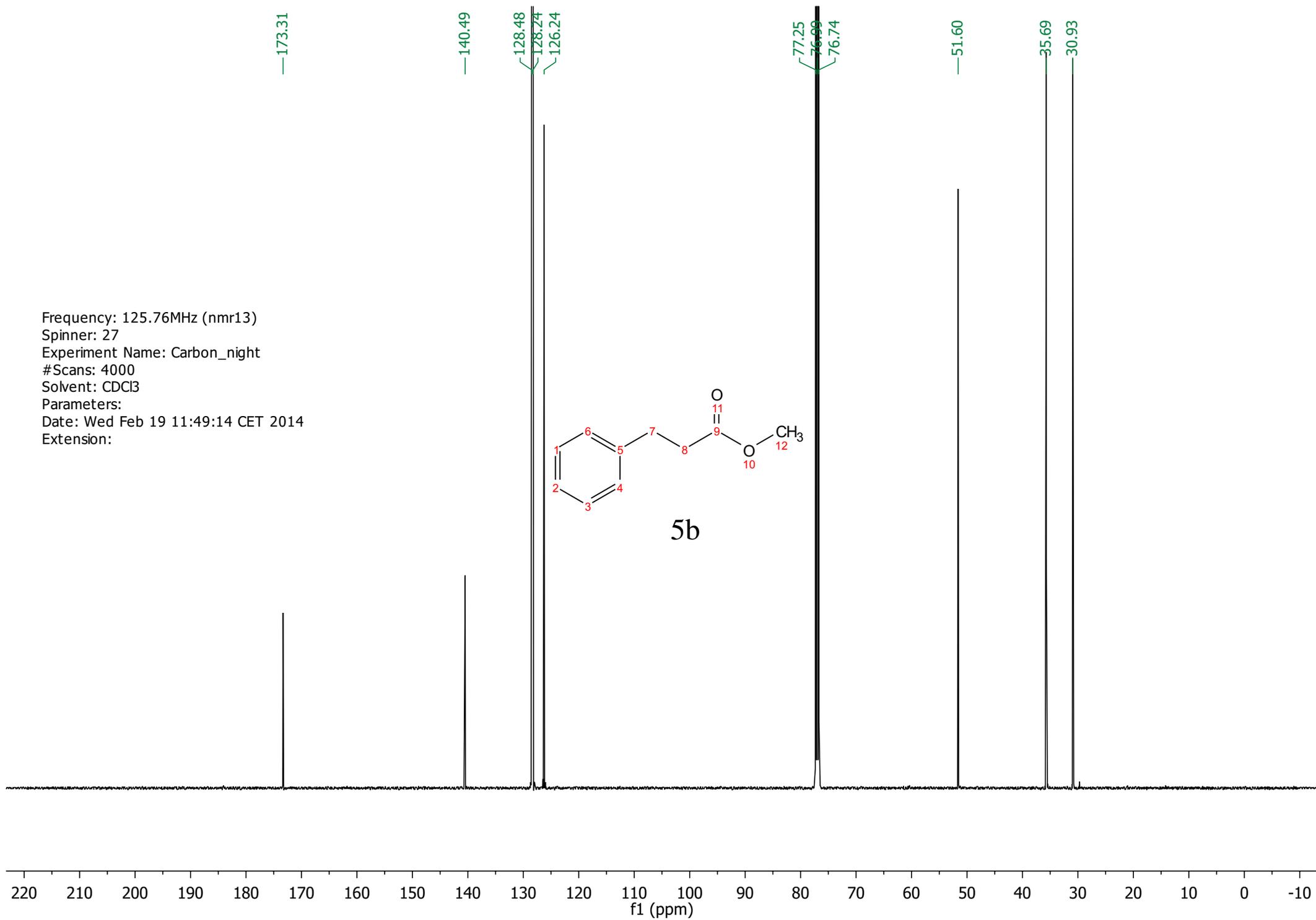
Frequency: 500.13MHz (nmr13)
Spinner: 27
Experiment Name: Proton_day
#Scans: 16
Solvent: CDCl3
Parameters:
Date: Wed Feb 19 08:44:08 CET 2014
Extension:



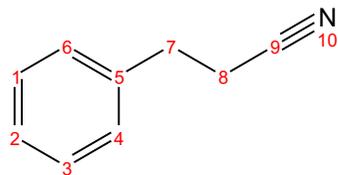
Frequency: 125.76MHz (nmr13)
Spinner: 27
Experiment Name: Carbon_night
#Scans: 4000
Solvent: CDCl3
Parameters:
Date: Wed Feb 19 11:49:14 CET 2014
Extension:



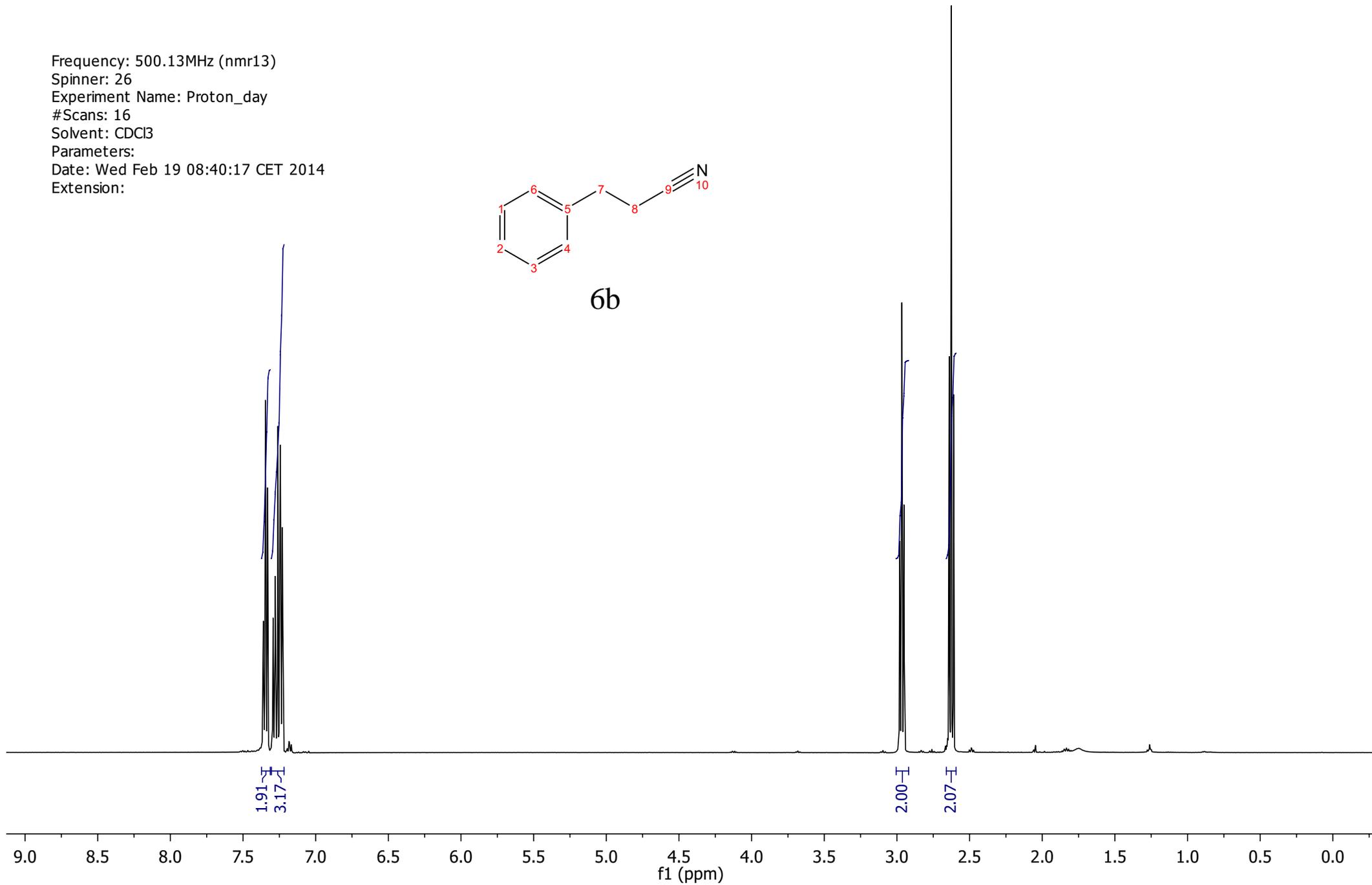
5b



Frequency: 500.13MHz (nmr13)
Spinner: 26
Experiment Name: Proton_day
#Scans: 16
Solvent: CDCl3
Parameters:
Date: Wed Feb 19 08:40:17 CET 2014
Extension:



6b



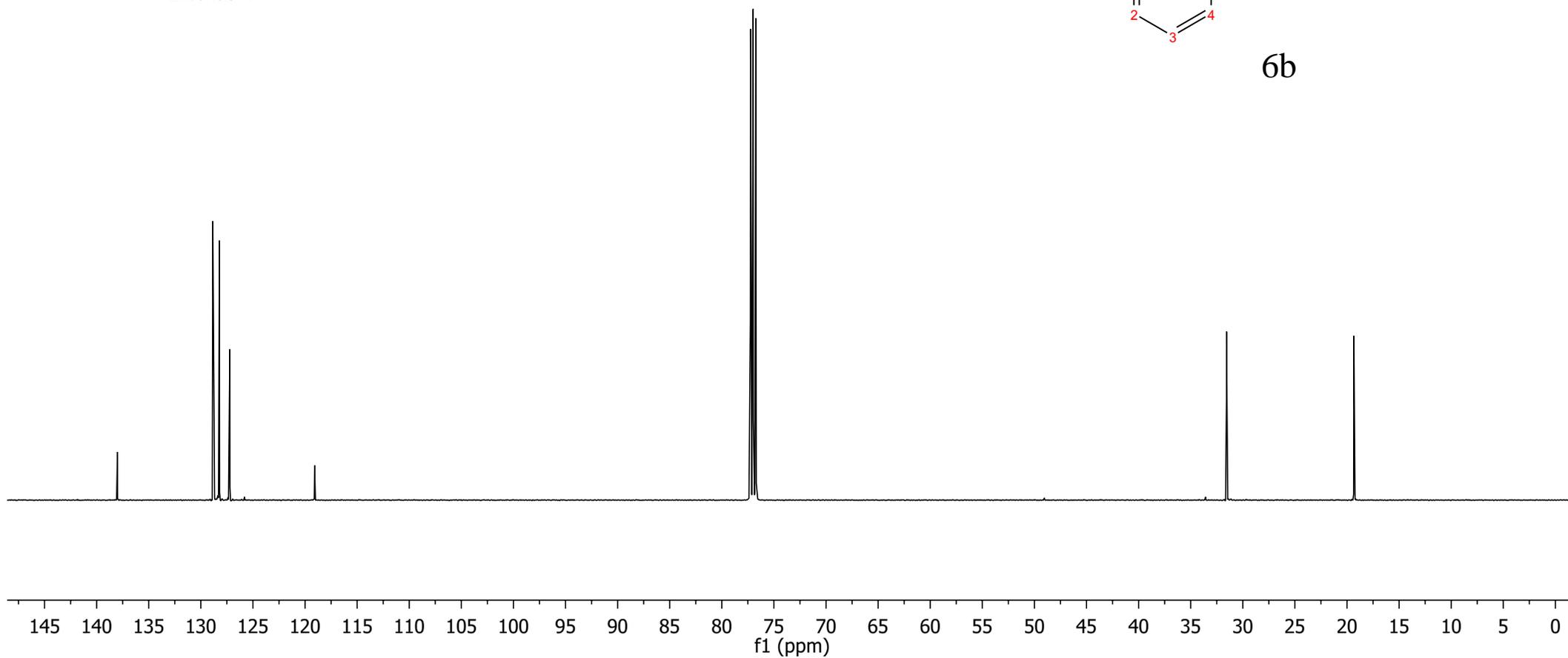
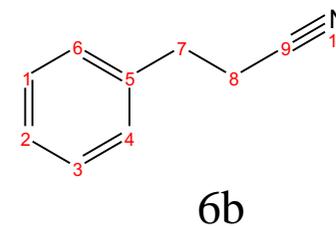
—138.01
128.85
128.33
128.22
127.22
—119.08

77.25
76.99
76.74

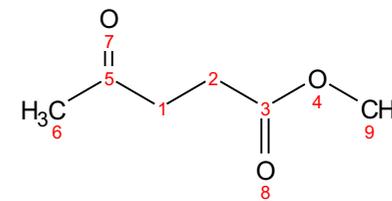
—31.56

—19.34

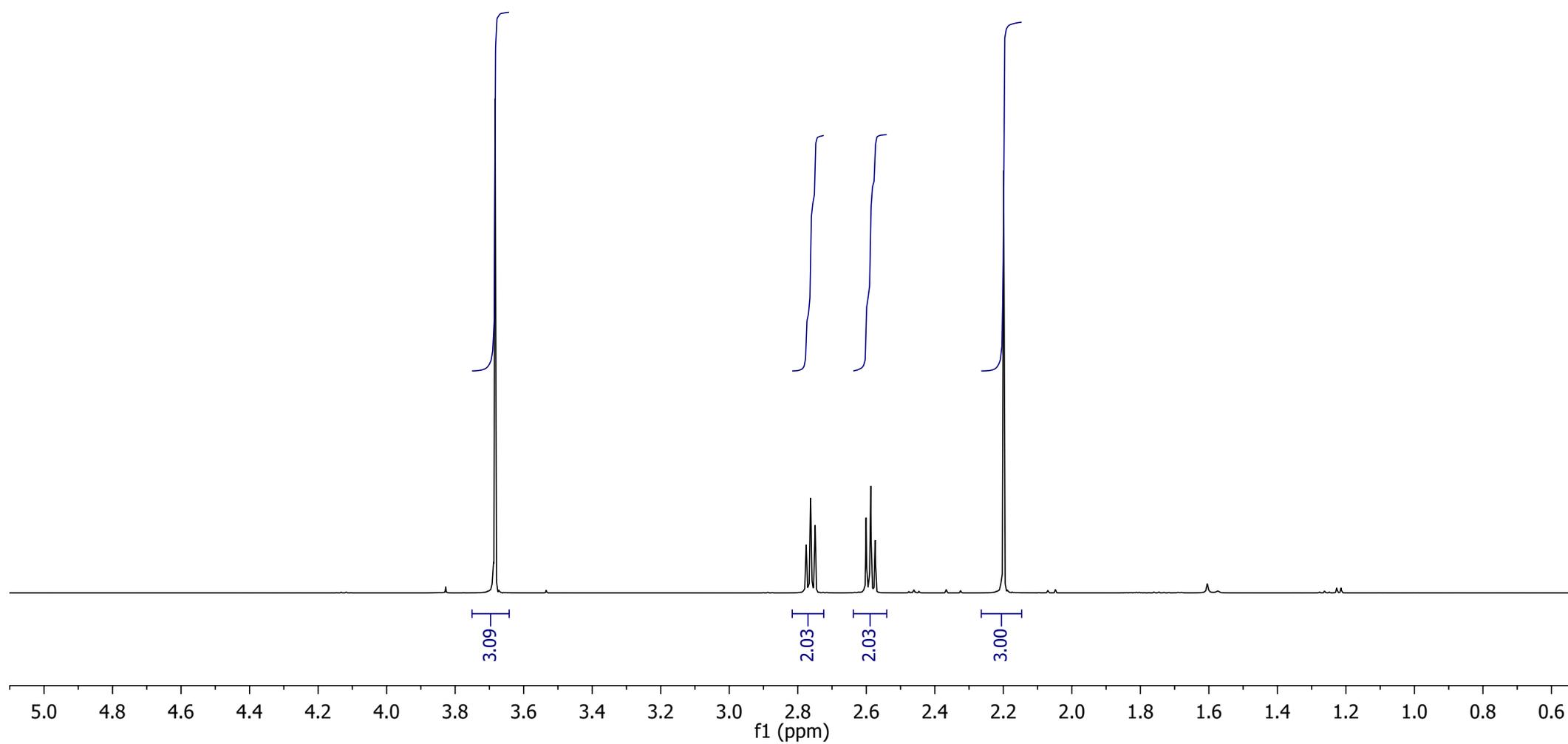
Frequency: 125.76MHz (nmr13)
Spinner: 26
Experiment Name: Carbon_night
#Scans: 4000
Solvent: CDCl3
Parameters:
Date: Wed Feb 19 11:49:00 CET 2014
Extension:



Frequency: 500.13MHz (nmr13)
Spinner: 75
Experiment Name: Proton_day
#Scans: 16
Solvent: CDCl3
Parameters:
Date: Tue Mar 11 08:54:42 CET 2014
Extension:



7b



—206.54

—173.13

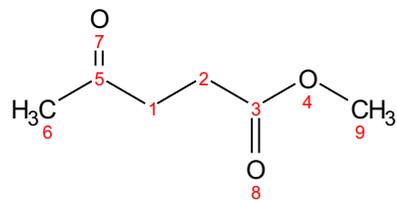
—51.72

—37.88

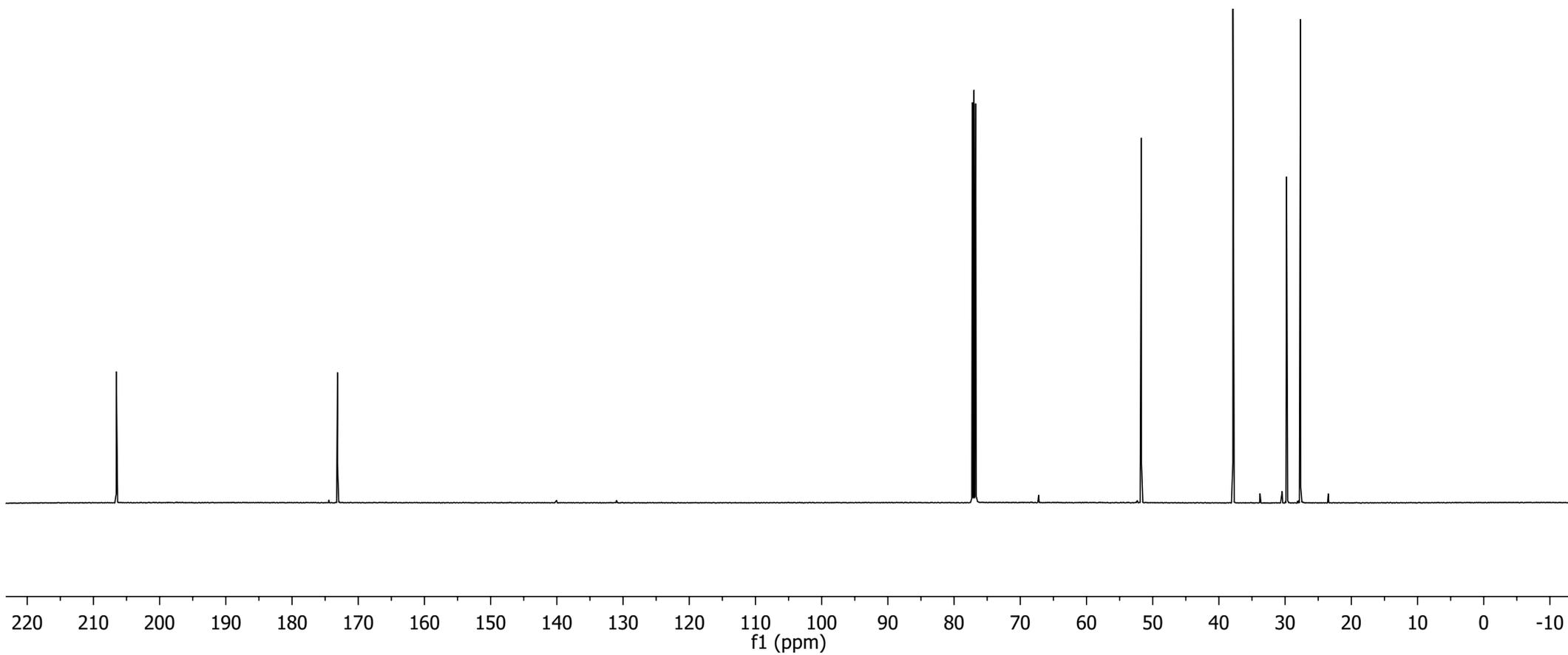
—29.78

—27.67

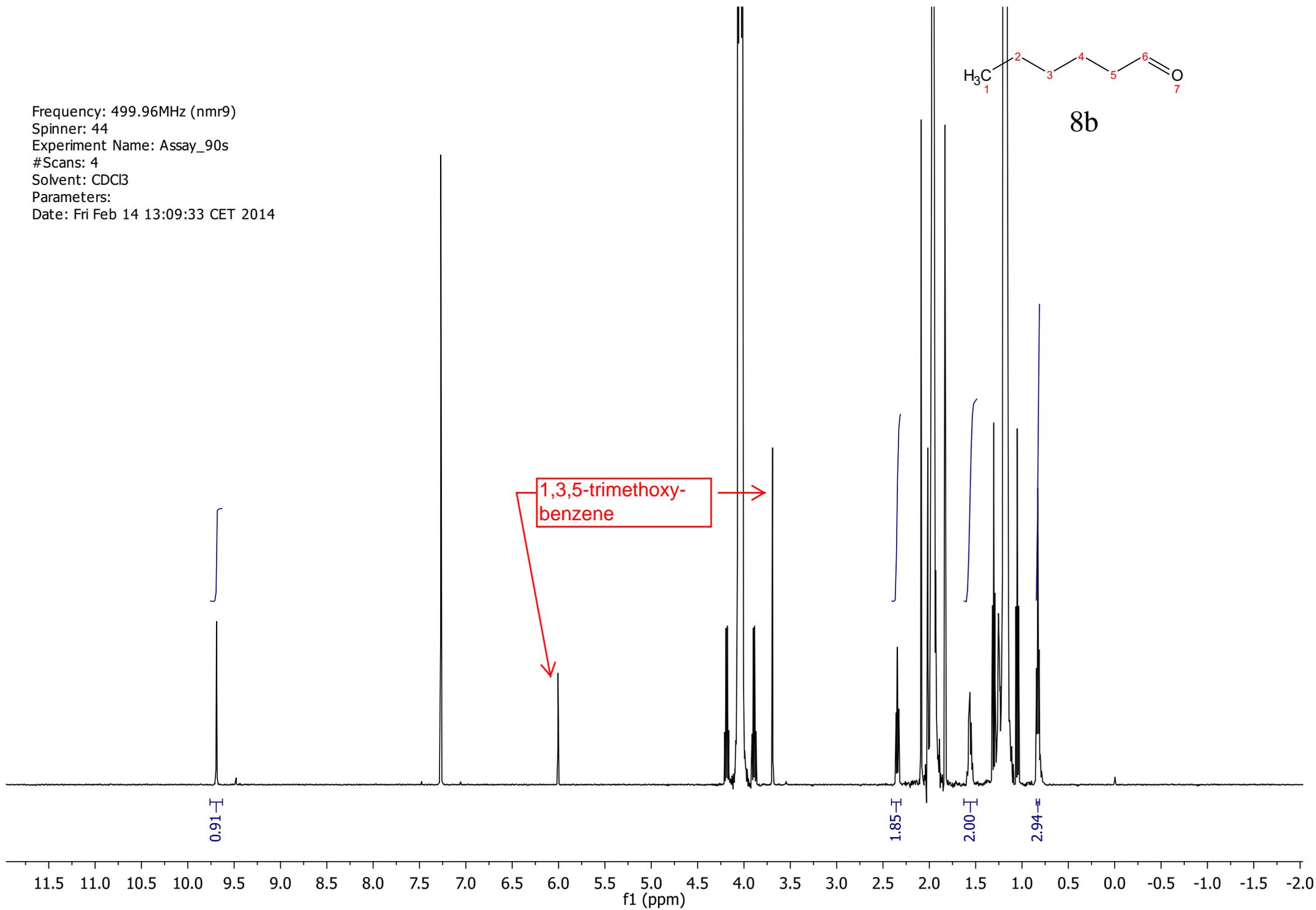
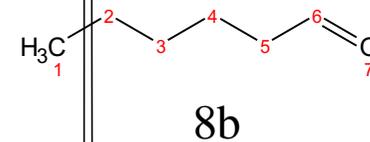
Frequency: 125.76MHz (nmr13)
Spinner: 27
Experiment Name: Carbon_night
#Scans: 4000
Solvent: CDCl3
Parameters:
Date: Thu Mar 20 08:14:49 CET 2014
Extension:



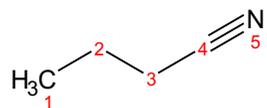
7b



Frequency: 499.96MHz (nmr9)
Spinner: 44
Experiment Name: Assay_90s
#Scans: 4
Solvent: CDCl3
Parameters:
Date: Fri Feb 14 13:09:33 CET 2014



Frequency: 500.13MHz (nmr13)
Spinner: 71
Experiment Name: Assay_90s
#Scans: 4
Solvent: CDCl3
Parameters:
Date: Mon Mar 10 10:24:24 CET 2014
Extension:

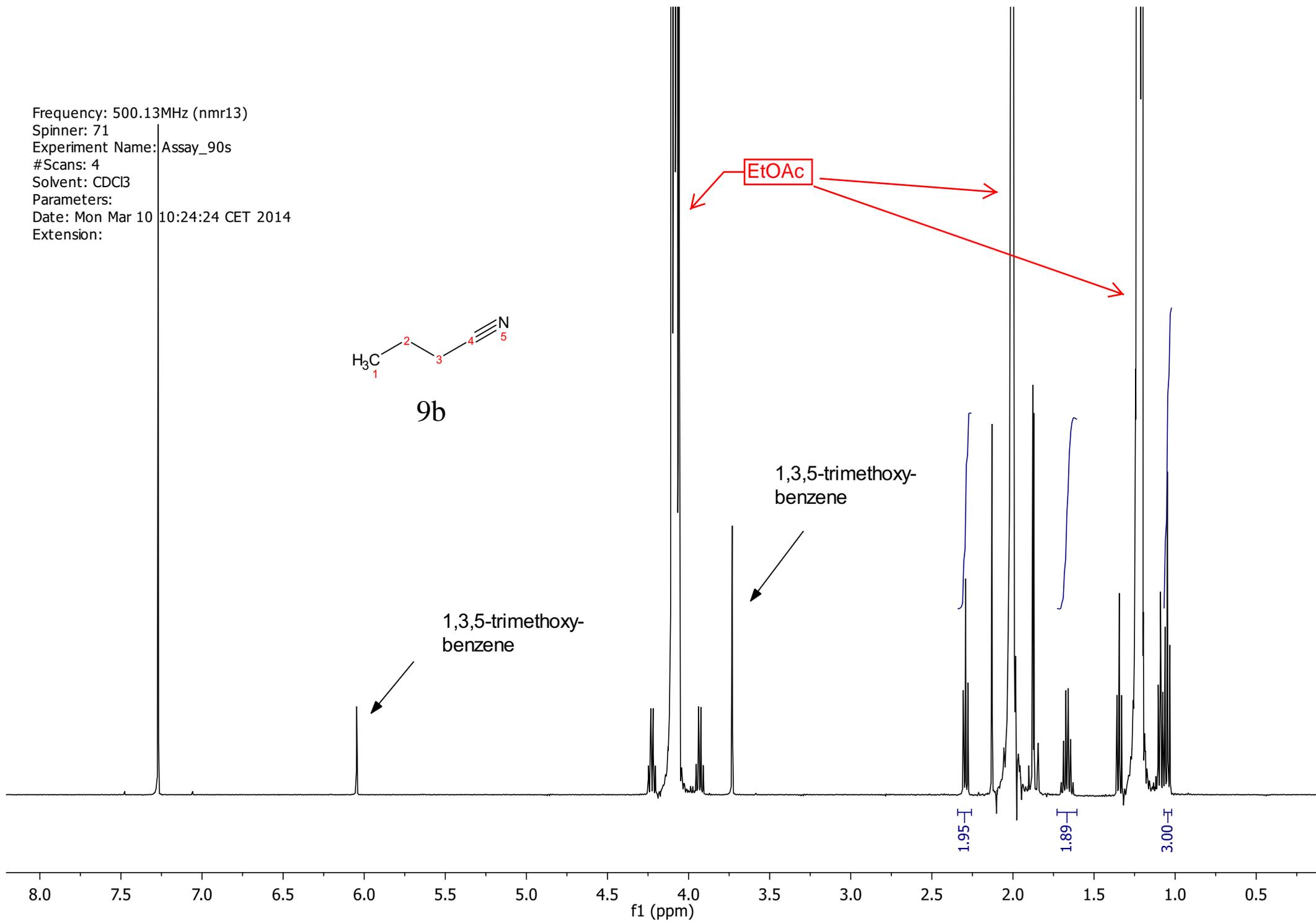


9b

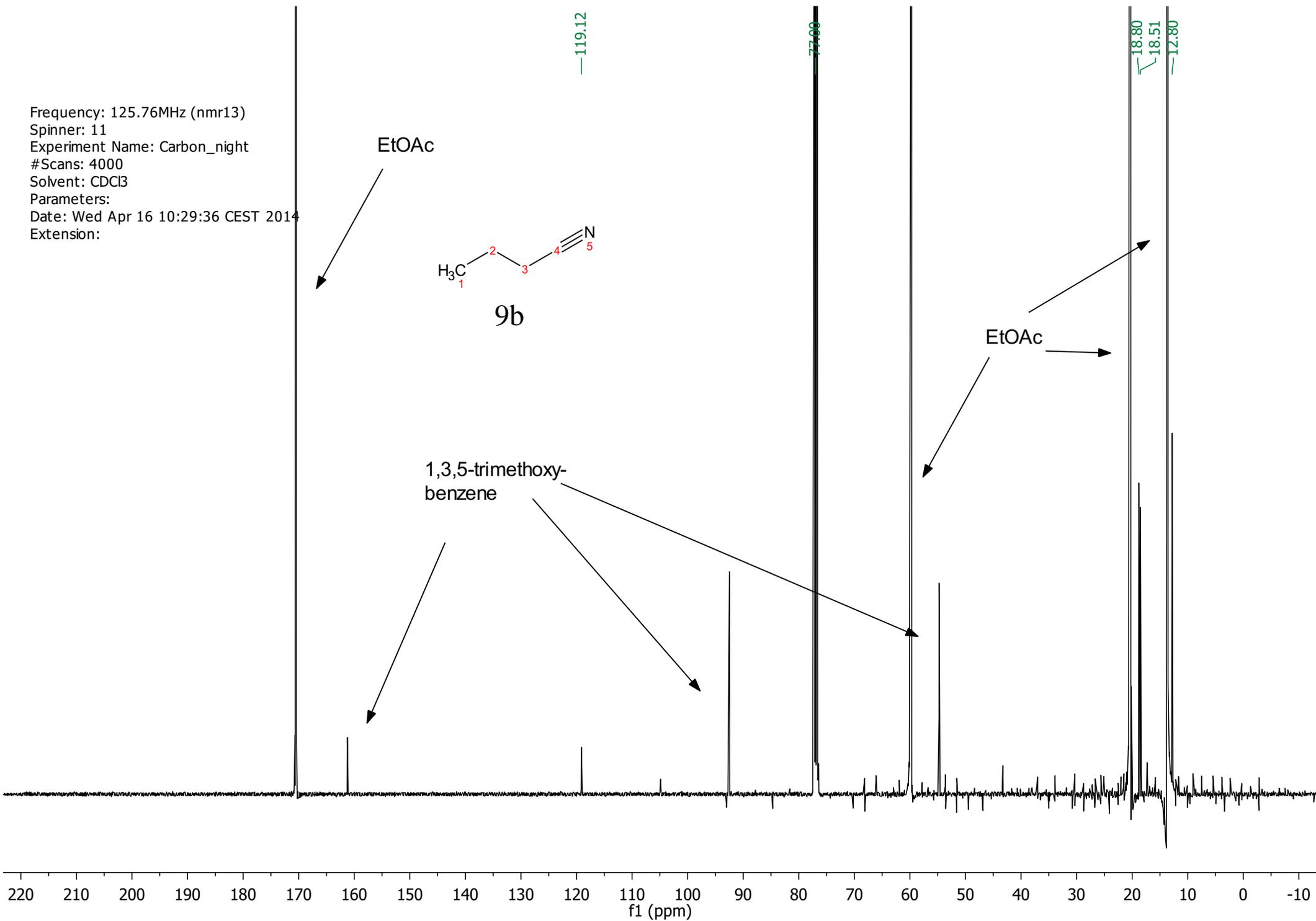
EtOAc

1,3,5-trimethoxy-
benzene

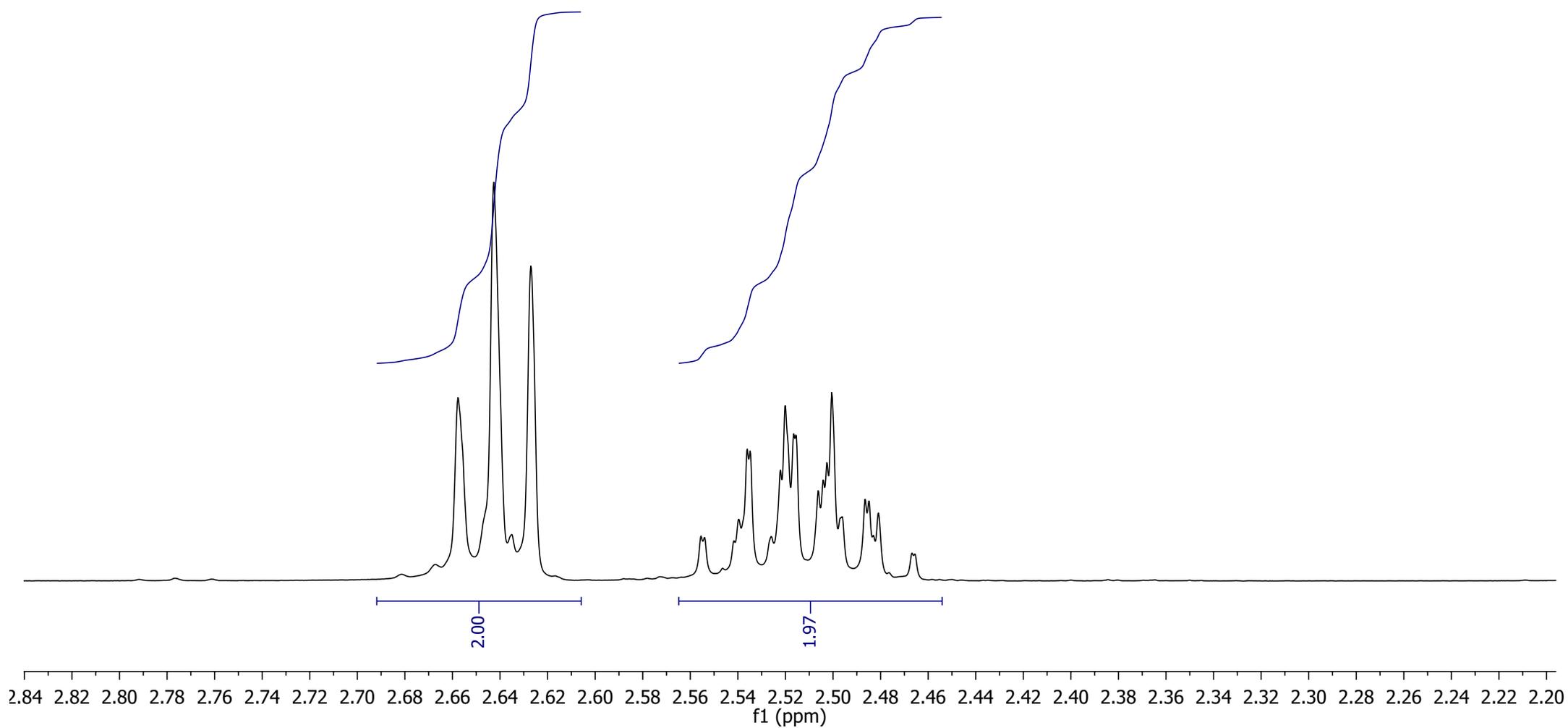
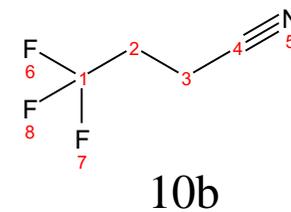
1,3,5-trimethoxy-
benzene



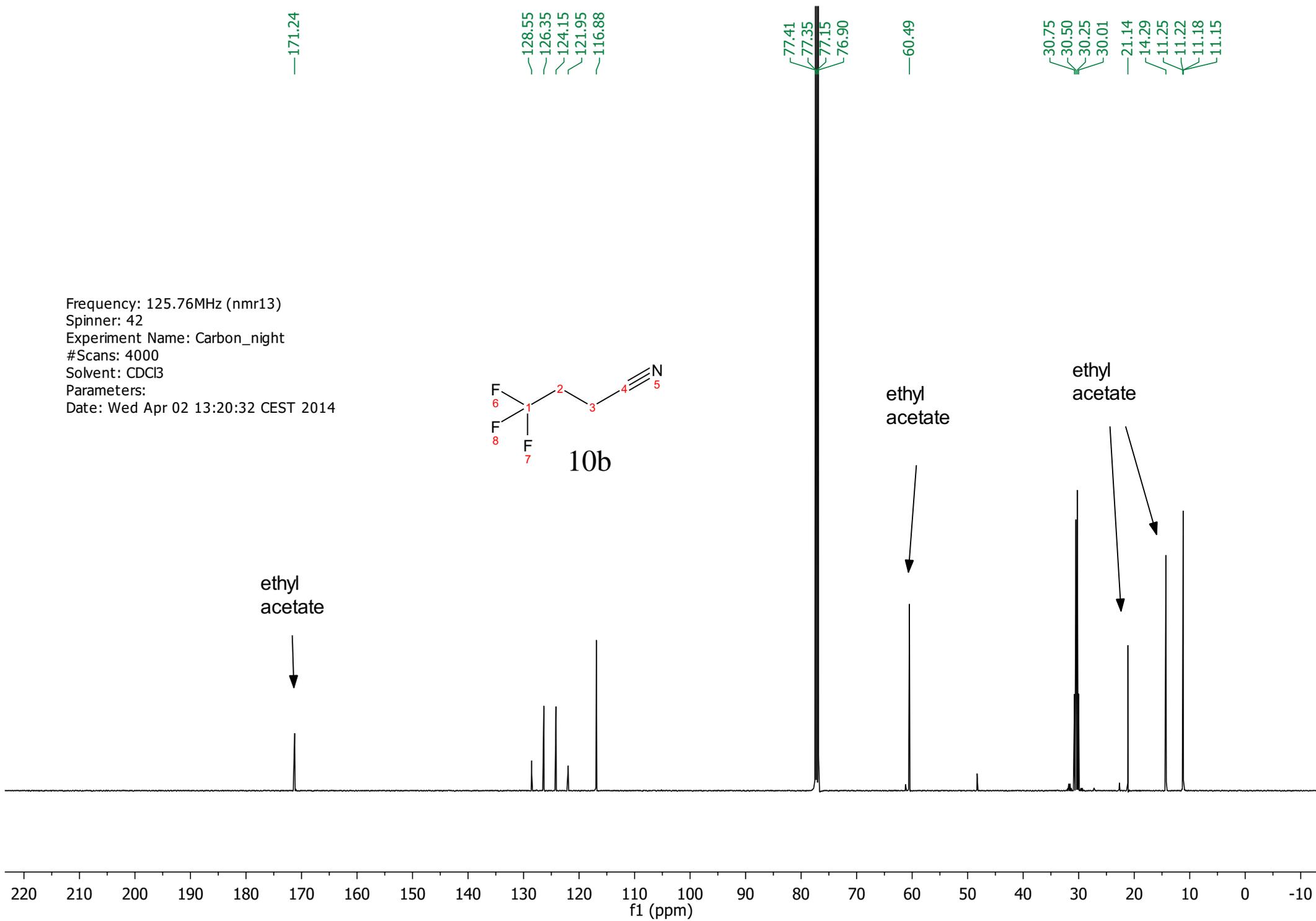
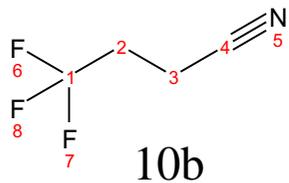
Frequency: 125.76MHz (nmr13)
Spinner: 11
Experiment Name: Carbon_night
#Scans: 4000
Solvent: CDCl3
Parameters:
Date: Wed Apr 16 10:29:36 CEST 2014
Extension:



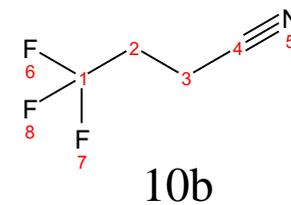
Frequency: 500.13MHz (nmr13)
Spinner: 7
Experiment Name: Proton_day
#Scans: 16
Solvent: CDCl3
Parameters:
Date: Wed Apr 02 10:20:04 CEST 2014



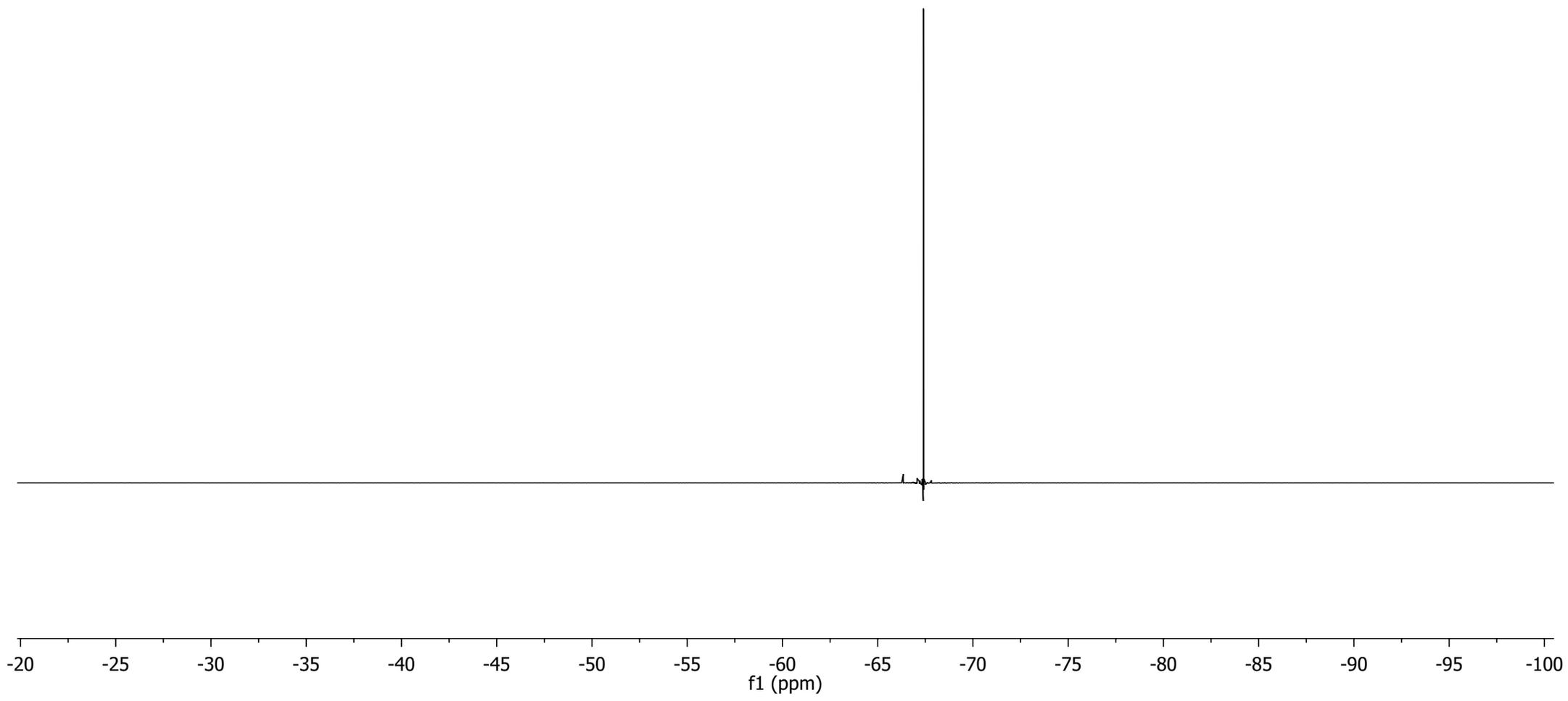
Frequency: 125.76MHz (nmr13)
Spinner: 42
Experiment Name: Carbon_night
#Scans: 4000
Solvent: CDCl3
Parameters:
Date: Wed Apr 02 13:20:32 CEST 2014



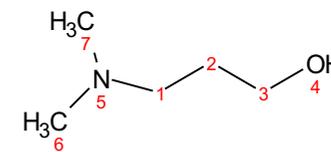
Frequency: 470.59MHz (nmr13)
Spinner: 7
Experiment Name: Fluorine_day
#Scans: 32
Solvent: CDCl3
Parameters:
Date: Wed Apr 02 10:20:27 CEST 2014
Extension: 200mg



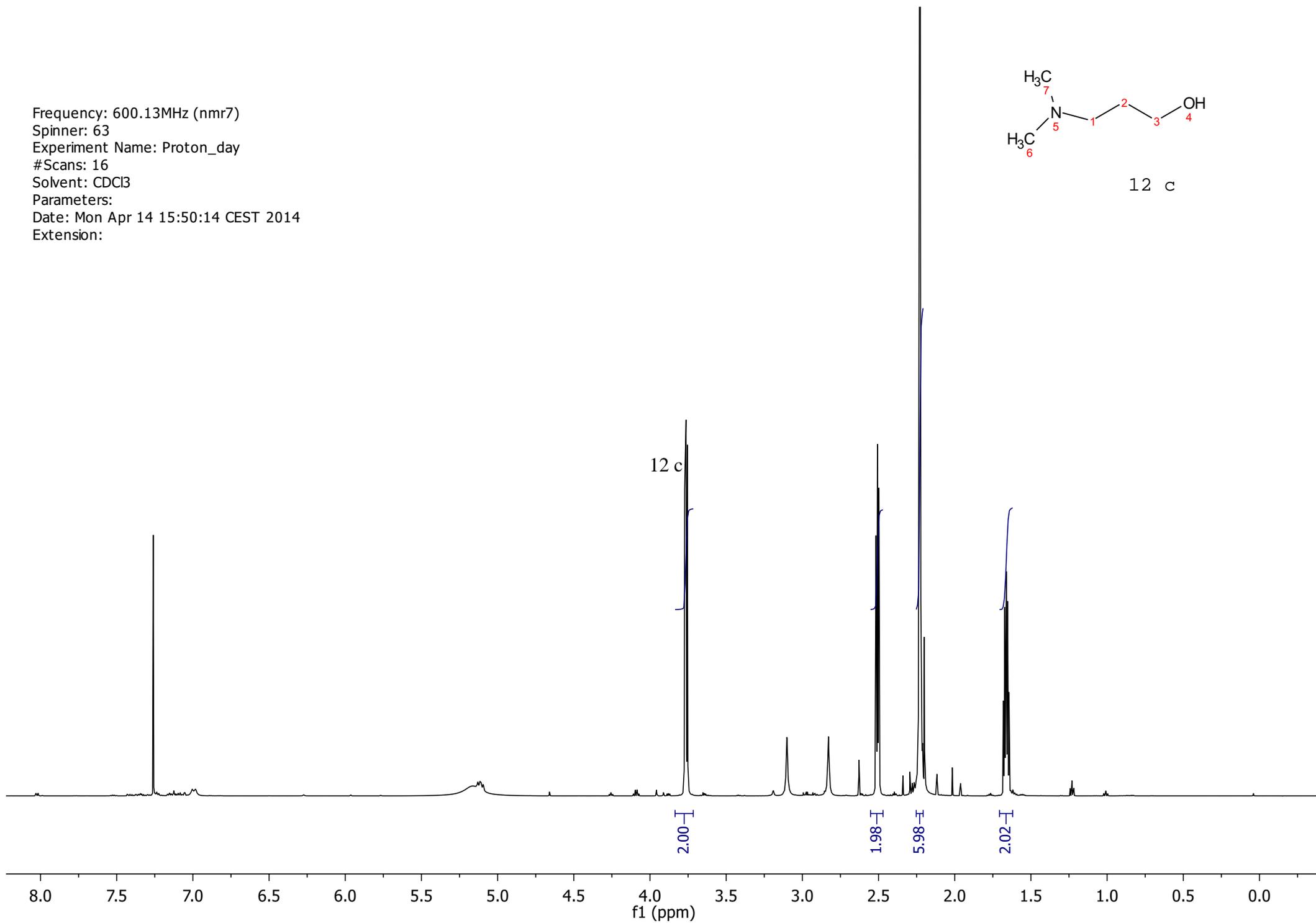
-67.40



Frequency: 600.13MHz (nmr7)
Spinner: 63
Experiment Name: Proton_day
#Scans: 16
Solvent: CDCl3
Parameters:
Date: Mon Apr 14 15:50:14 CEST 2014
Extension:



12 c



Frequency: 150.90MHz (nmr7)
Spinner: 63
Experiment Name: Carbon_night
#Scans: 4000
Solvent: CDCl3
Parameters:
Date: Mon Apr 14 15:50:20 CEST 2014
Extension:

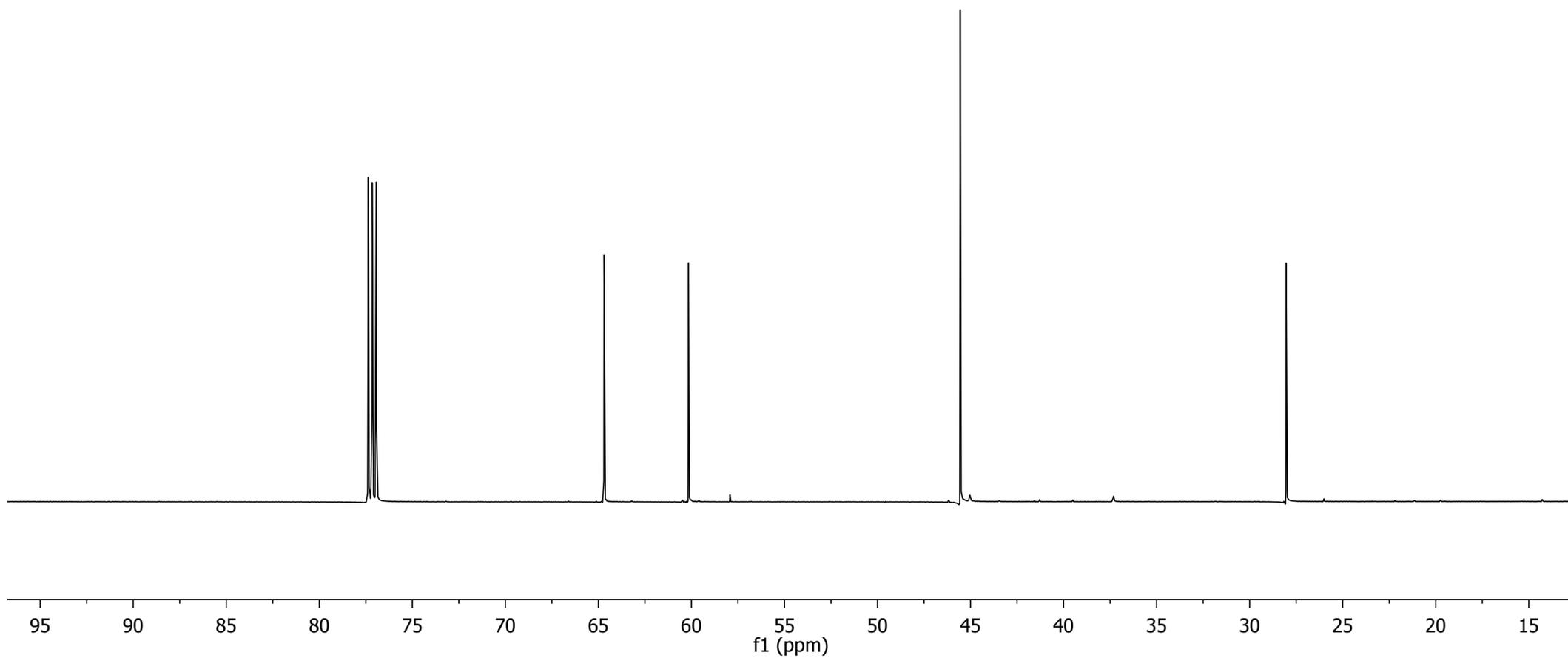
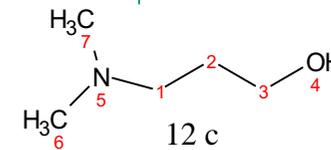
77.37
77.15
76.94

64.70

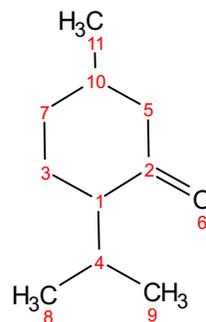
60.15

45.55

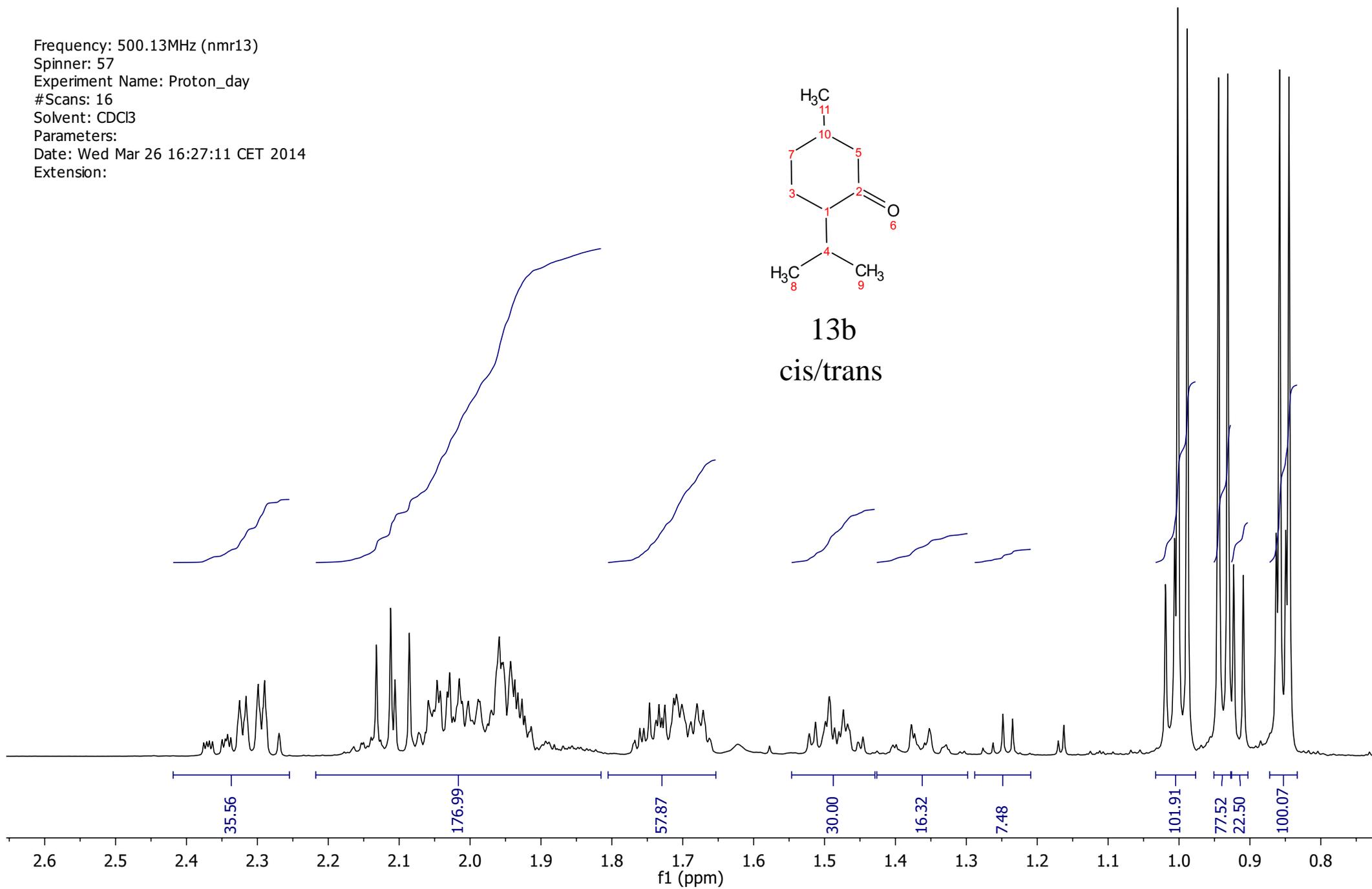
28.04



Frequency: 500.13MHz (nmr13)
Spinner: 57
Experiment Name: Proton_day
#Scans: 16
Solvent: CDCl3
Parameters:
Date: Wed Mar 26 16:27:11 CET 2014
Extension:



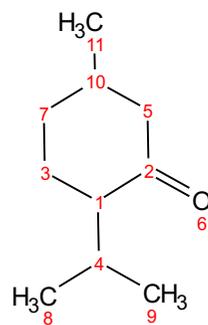
13b
cis/trans



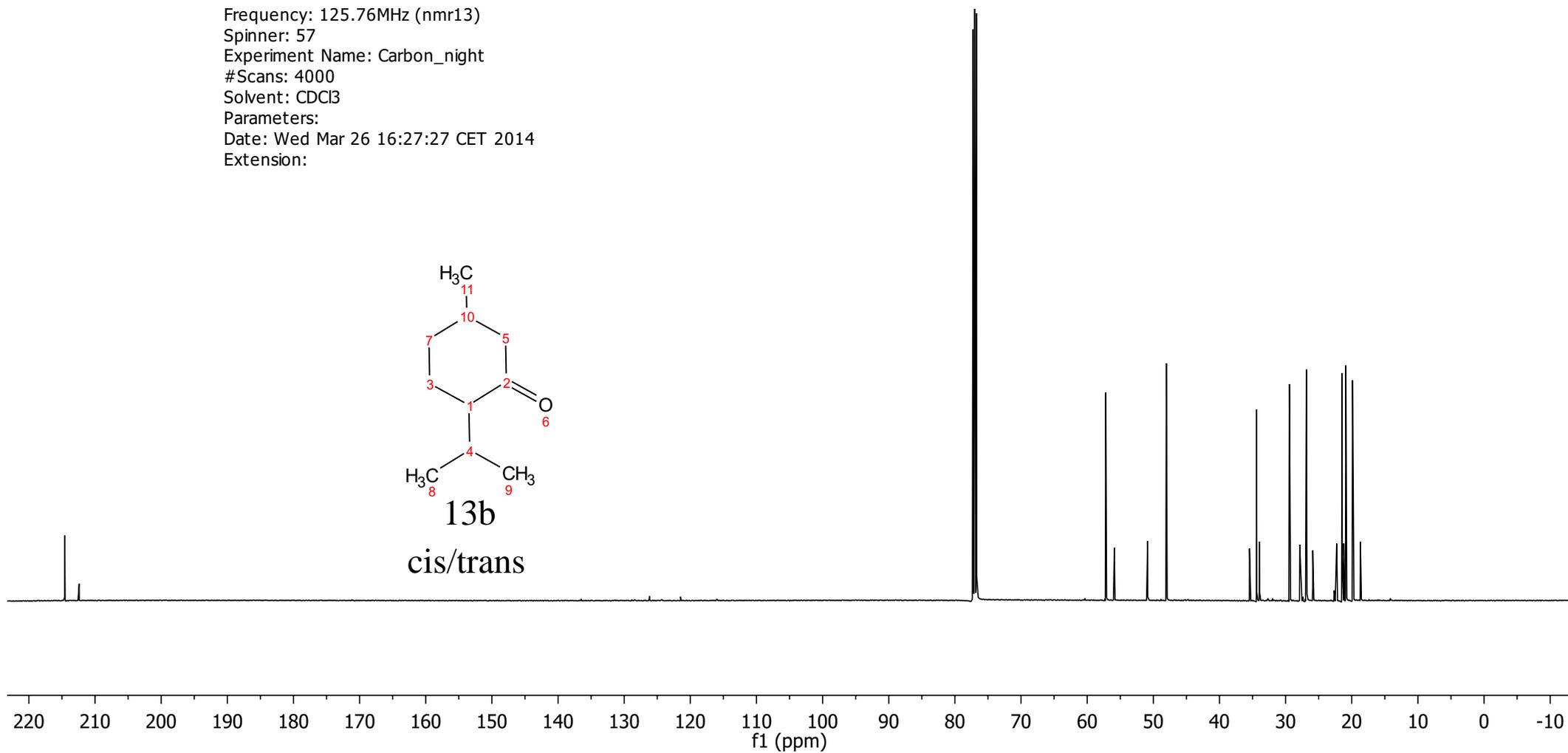
~214.58
~212.40

57.19
55.89
50.87
48.03
35.46
34.39
33.93
29.43
27.86
26.91
26.85
25.89
22.28
21.45
21.21
20.89
19.88
18.69

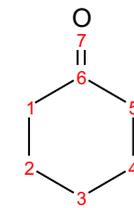
Frequency: 125.76MHz (nmr13)
Spinner: 57
Experiment Name: Carbon_night
#Scans: 4000
Solvent: CDCl3
Parameters:
Date: Wed Mar 26 16:27:27 CET 2014
Extension:



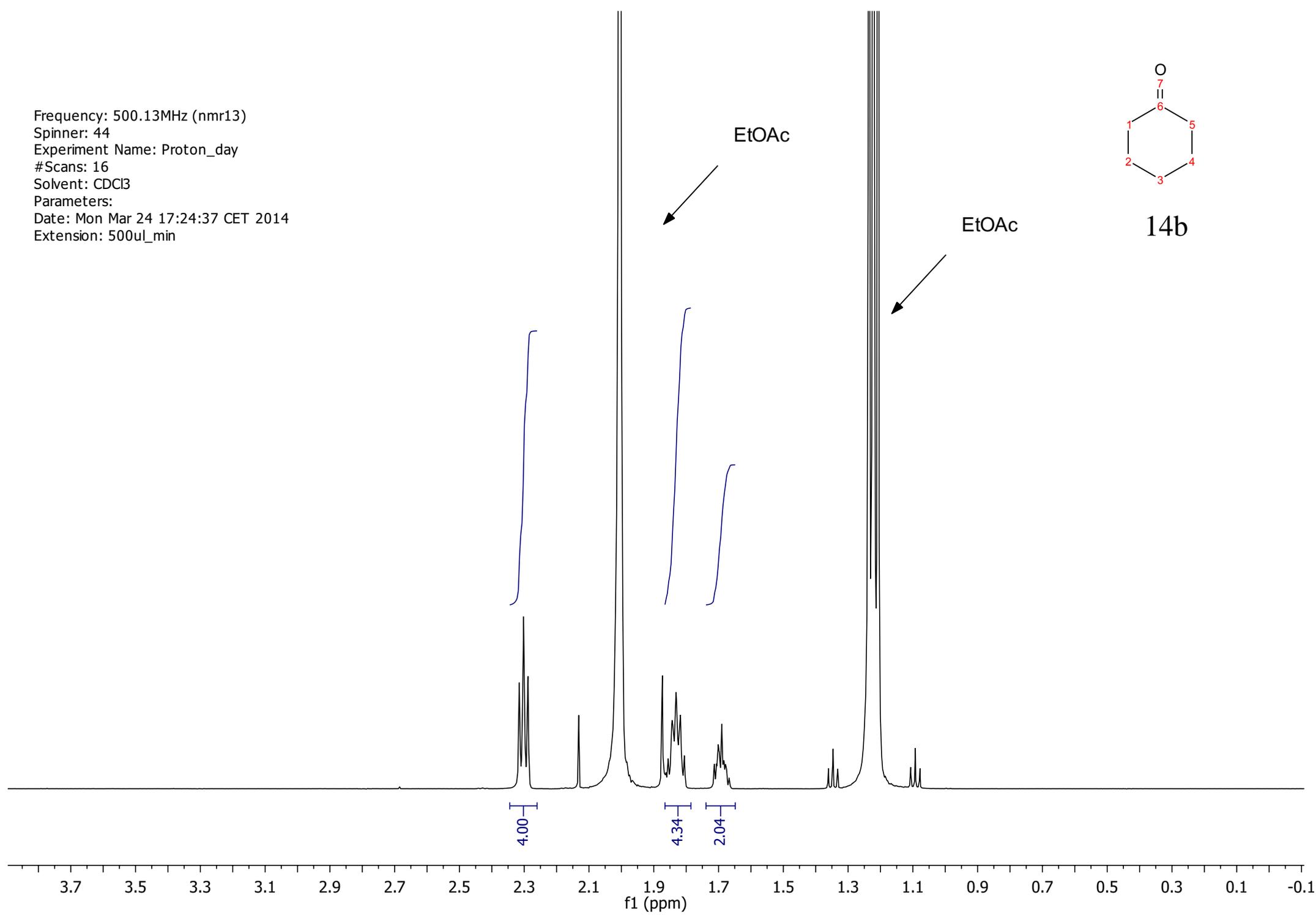
13b
cis/trans



Frequency: 500.13MHz (nmr13)
Spinner: 44
Experiment Name: Proton_day
#Scans: 16
Solvent: CDCl3
Parameters:
Date: Mon Mar 24 17:24:37 CET 2014
Extension: 500ul_min



14b



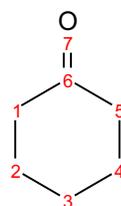
—211.83

—41.95

~27.03

~25.01

Frequency: 125.76MHz (nmr13)
Spinner: 32
Experiment Name: Carbon_night
#Scans: 4000
Solvent: CDCl3
Parameters:
Date: Thu Apr 24 16:16:05 CEST 2014
Extension: 500ul



14b

